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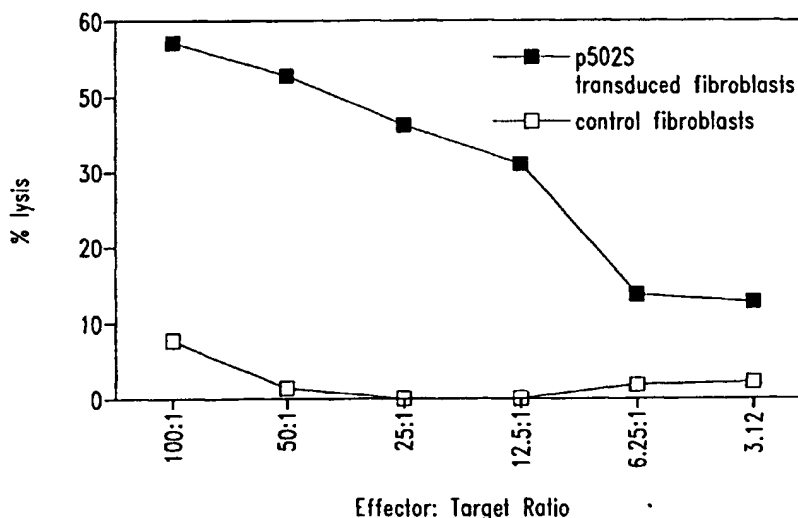
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### 5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for  
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress  
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but  
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate  
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### 30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.



Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5                Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10              Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15              Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

20              Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

25              Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

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The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

30

embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that  
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)  
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as  
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed  
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The  
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure  
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5        Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

10        Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

15        Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20        Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25        Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30        SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

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SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17  
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12  
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SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13  
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SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24  
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SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58  
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63  
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63  
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SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14  
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14  
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SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16  
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SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48  
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55  
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2  
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6  
30 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858  
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860  
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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- SEQ ID NO: 41 is the determined cDNA sequence for P5
- SEQ ID NO: 42 is the determined cDNA sequence for P8
- SEQ ID NO: 43 is the determined cDNA sequence for P9
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- SEQ ID NO: 46 is the determined cDNA sequence for P29
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- SEQ ID NO: 48 is the determined cDNA sequence for P34
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- SEQ ID NO: 56 is the determined cDNA sequence for P53
- SEQ ID NO: 57 is the determined cDNA sequence for P55
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SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304

SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

SEQ ID NO: 115 is the determined cDNA sequence for P89

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SEQ ID NO: 117 is the determined cDNA sequence for P92

SEQ ID NO: 118 is the determined cDNA sequence for P95

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SEQ ID NO: 133 is the determined cDNA sequence for P156



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SEQ ID NO: 165 is the determined cDNA sequence for P195

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SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876  
SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884  
SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896  
SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761  
30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762  
SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766  
SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteasome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15 374.
- SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.



- SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:397 is the cDNA sequence for PAP.
- SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.
- SEQ ID NO:399 is the cDNA sequence for hTGR.
- 5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.
- SEQ ID NO:401 is the cDNA sequence for 22545.
- SEQ ID NO:402 is the cDNA sequence for 22547.
- SEQ ID NO:403 is the cDNA sequence for 22548.
- SEQ ID NO:404 is the cDNA sequence for 22550.
- 10 SEQ ID NO:405 is the cDNA sequence for 22551.
- SEQ ID NO:406 is the cDNA sequence for 22552.
- SEQ ID NO:407 is the cDNA sequence for 22553.
- SEQ ID NO:408 is the cDNA sequence for 22558.
- SEQ ID NO:409 is the cDNA sequence for 22562.
- 15 SEQ ID NO:410 is the cDNA sequence for 22565.
- SEQ ID NO:411 is the cDNA sequence for 22567.
- SEQ ID NO:412 is the cDNA sequence for 22568.
- SEQ ID NO:413 is the cDNA sequence for 22570.
- SEQ ID NO:414 is the cDNA sequence for 22571.
- 20 SEQ ID NO:415 is the cDNA sequence for 22572.
- SEQ ID NO:416 is the cDNA sequence for 22573.
- SEQ ID NO:417 is the cDNA sequence for 22573.
- SEQ ID NO:418 is the cDNA sequence for 22575.
- SEQ ID NO:419 is the cDNA sequence for 22580.
- 25 SEQ ID NO:420 is the cDNA sequence for 22581.
- SEQ ID NO:421 is the cDNA sequence for 22582.
- SEQ ID NO:422 is the cDNA sequence for 22583.
- SEQ ID NO:423 is the cDNA sequence for 22584.
- SEQ ID NO:424 is the cDNA sequence for 22585.
- 30 SEQ ID NO:425 is the cDNA sequence for 22586.
- SEQ ID NO:426 is the cDNA sequence for 22587.
- SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
5 SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
10 SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
15 SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
20 SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.  
SEQ ID NO:451 is the cDNA sequence for 23614.  
25 SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
30 SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

5 SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
15 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
25 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

30 SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

- SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.
- SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.
- SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.
- SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.
- SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.
- SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.
- SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.
- SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.
- SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.
- SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-550 are epitopes of P501S.
- SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

## DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

## PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also  
5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the  
10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions  
15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The  
20 term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local  
25 regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the  
30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into



a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector  
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for  
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.  
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary  
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane  
30 vesicle). The preparation and use of such systems is well known in the art.

## PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997*).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g., the first N-terminal 100-110 amino acids*), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene 43:265-292, 1986*). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology 10:795-798, 1992*). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its



original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector  
5 that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an  
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding  
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals  
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the  
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are  
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.  
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to  
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by  
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the  
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard  
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5           It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or  
10   linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent  
15   No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating  
20   compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of  
25   a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

30           Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated  
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific  
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a  
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell  
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of  
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate-specific protein-specific T cells may be expanded using  
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide  
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

10

#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds  
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally  
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the  
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression  
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA



or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12; may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10 ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent  
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release  
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix  
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

20 Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the  
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or  
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

*Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface  
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone  
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into  
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this  
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II  
25 MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*  
30 *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells  
5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of  
10 the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical  
15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.  
20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react  
25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not  
30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate  
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*  
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,  
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies  
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back  
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established  
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%  
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-  
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active  
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be  
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or  
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the  
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g., Harlow and Lane, 5 Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized  
10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,  
15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full  
20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or  
25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization"  
30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20<sup>TM</sup> (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by



assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains  
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of  
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group  
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a  
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is  
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest  
30 to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue,  
5 and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or  
10 greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or  
15 polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

20 Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

25 As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or  
30 alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

## DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For  
5 example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or  
10 indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or  
15 hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate  
10 tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA  
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into  
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$   
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As  
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with  
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA  
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and  
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,  
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA



library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show  
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid  
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided  
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating  
20 sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in  
30 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA<sup>+</sup> RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue  
5 (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found  
10 to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other  
15 tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of  
20 prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

25 RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH  
prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors  
30 and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following  
5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues  
10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in  
15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in  
20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and  
25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was  
30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

20

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences  
5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the  
10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-  
15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA  
20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary  
25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a  
30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.



An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the  
5 cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence  
10 being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no  
15 significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479.  
20 The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.  
25

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the  
30 genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5           6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

          Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID  
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco  
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ( $5 \times$   
20  $10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

          P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb  
25 tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in  
30 Figure 1.

          This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice  
5 were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2  
10 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on  
15 the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described  
20 by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured  
25 in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were  
30 restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

##### 10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100  $\mu$ g P501S in the vector VR1012 either intramuscularly or intradermally. 15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at 20 least one naturally processed HLA-A2-restricted CTL epitope.

#### EXAMPLE 8

##### 25 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van 30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon



ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on  $10^4$  fibroblasts in the presence of 3  $\mu\text{g/ml}$  human  $\beta_2$ -microglobulin and 1  $\mu\text{g/ml}$  P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

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## EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES  
IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

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Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of  
5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a  
10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that  
15 specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S  
25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were  
30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40  
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as  
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-  
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

25

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in  
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-Iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

10

## EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS  
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which



expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV  
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

## EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY  
ANALYSIS

5

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened  
10 using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

15

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

20

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four  
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

## EXAMPLE 17

### PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

#### a) Expression in *E. coli*

15

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an  
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,  
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was  
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5           An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR  
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

          The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands  
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

          A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25           The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15  $\mu$ l of GenePorter was diluted in 500  $\mu$ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2  $\mu$ g of plasmid DNA that was diluted in 500  $\mu$ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### EXAMPLE 18

##### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

###### 20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to



generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

## Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

#### **b) Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception  
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat  
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal,  
20 breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,  
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal  
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

### 5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptrl; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptrl attached to a solid support. Rabbit monoclonal  
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal  
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

#### EXAMPLE 19

##### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of  
5 SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the  
10 following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was  
15 determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence  
20 using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as  
25 above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

30 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM



sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by  
5 SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma  
10 membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter  
15 plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with  
20 phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates  
25 were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

30 In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as  
5 described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were  
10 recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4  
15 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the  
20 probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

25

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

30

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein  
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,  
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a  
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,  
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one  
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,  
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.
- 5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.
- 10 14. A fusion protein comprising at least one polypeptide according to claim 1.
- 15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 17 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.
- 20 18. An isolated polynucleotide encoding a fusion protein according to claim 14.
- 25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:
- (a) a polypeptide according to claim 1;
  - (b) a polynucleotide according to claim 4;
  - (c) an antibody according to any one of claims 11-13;
  - 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;  
(b) a polynucleotide according to claim 4;  
(c) an antibody according to any one of claims 11-13;  
(d) a fusion protein according to claim 14; and  
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant  
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell  
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient,  
15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the  
25 cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is  
30 encoded by a polynucleotide sequence selected from the group consisting of:



(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5                    wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35.     A method according to claim 34, wherein the biological sample is  
10     blood or a fraction thereof.

36.     A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37.     A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i)     a polypeptide according to claim 1;

20            (ii)     a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii)    a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv)    an antigen presenting cell that expresses a polypeptide of (i) or (ii),

25            under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38.     An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;  
10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or  
15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) a polypeptide according to claim 1;  
(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,  
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate  
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient at a first point  
5 in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the  
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate  
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an  
30 oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,  
20 comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,  
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from  
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5                    54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10                   55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

                    56. A diagnostic kit, comprising:  
                    (a) one or more antibodies according to claim 11; and  
15                   (b) a detection reagent comprising a reporter group.

                    57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20                   58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

                    59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,  
25                   enzymes, biotin and dye particles.

                    60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is  
30                   encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 61; and

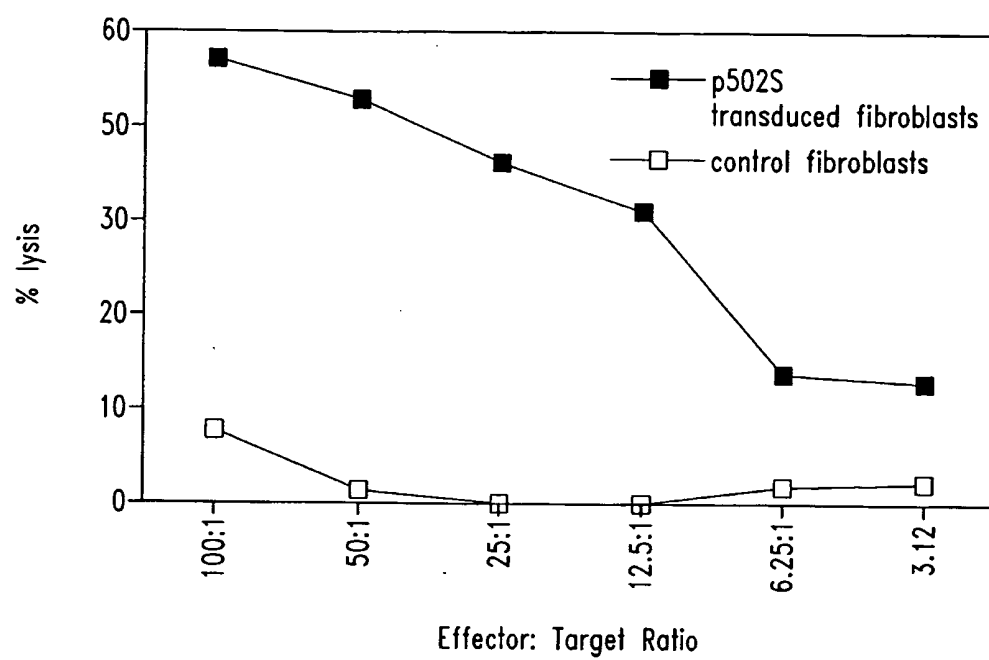
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

20

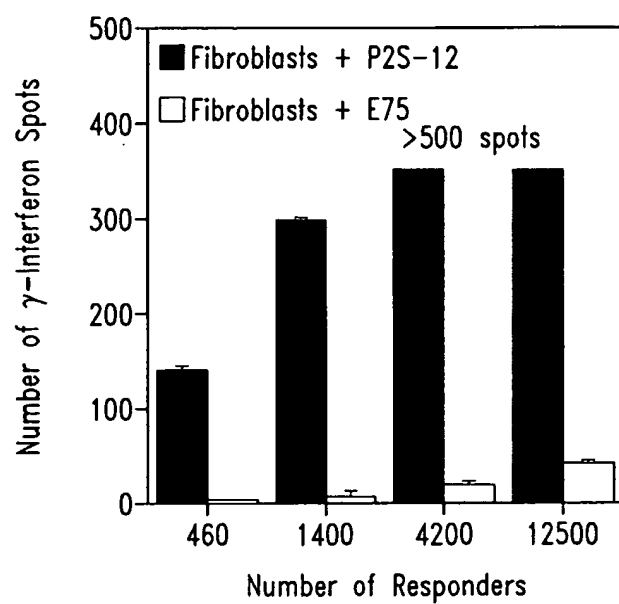
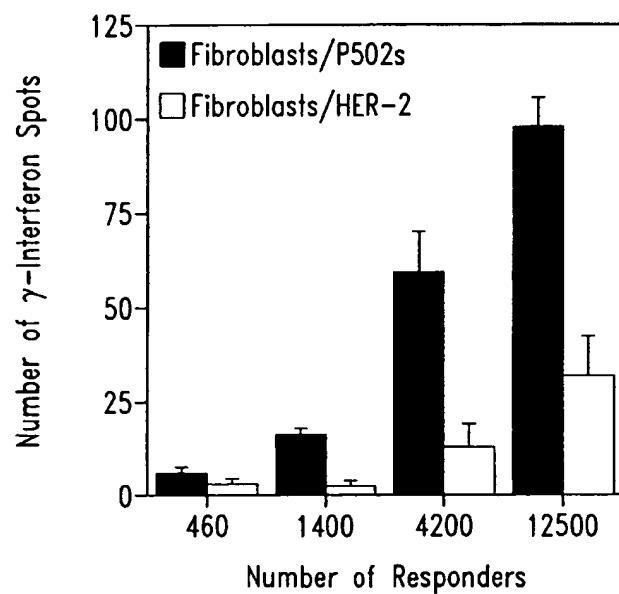
63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim

25 10.

*Fig. 1*



*Fig. 2A**Fig. 2B*

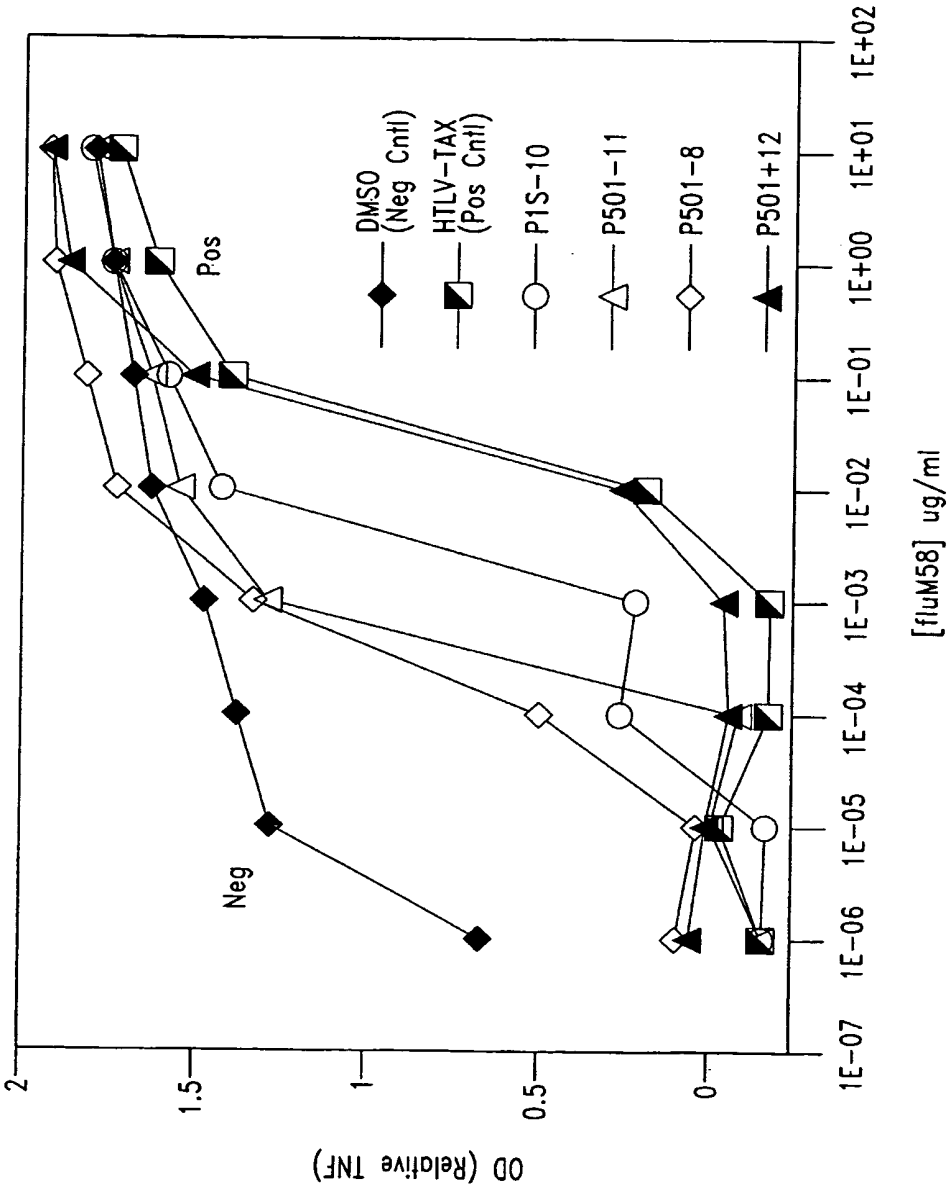
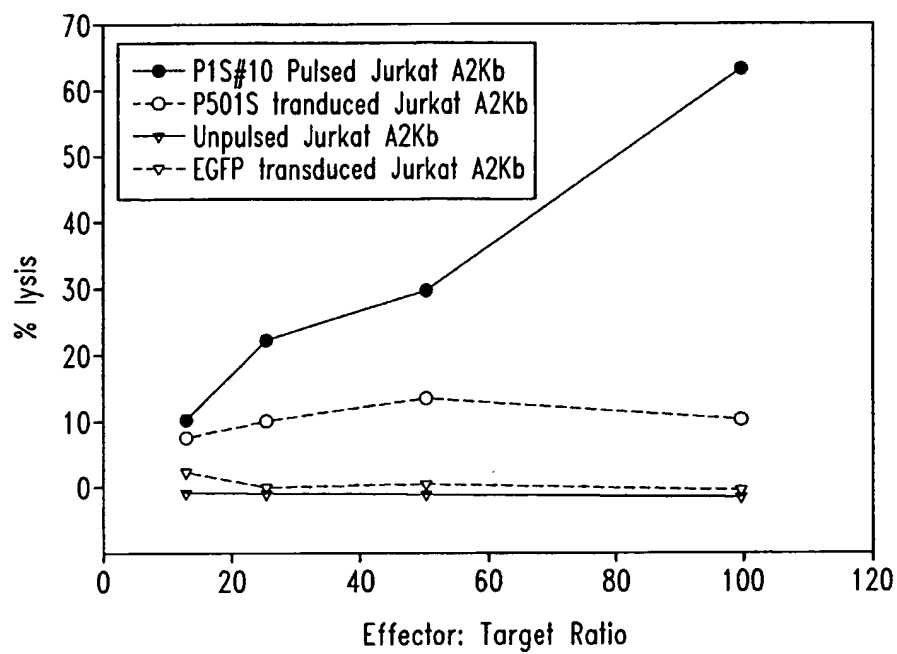
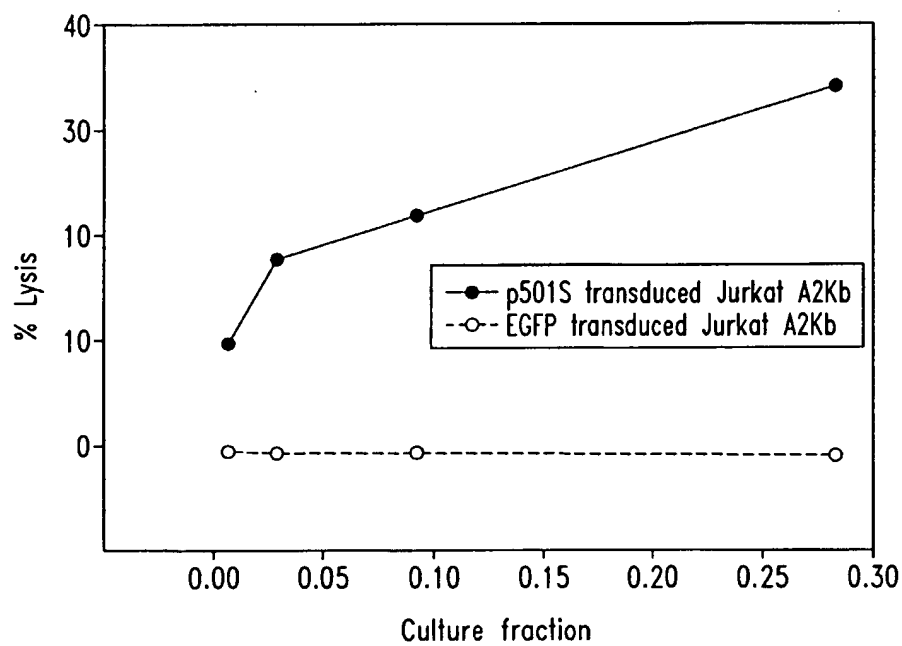
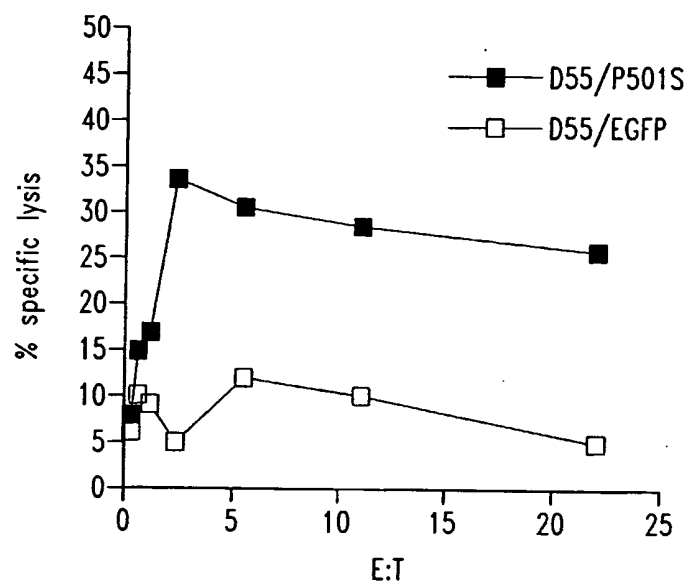
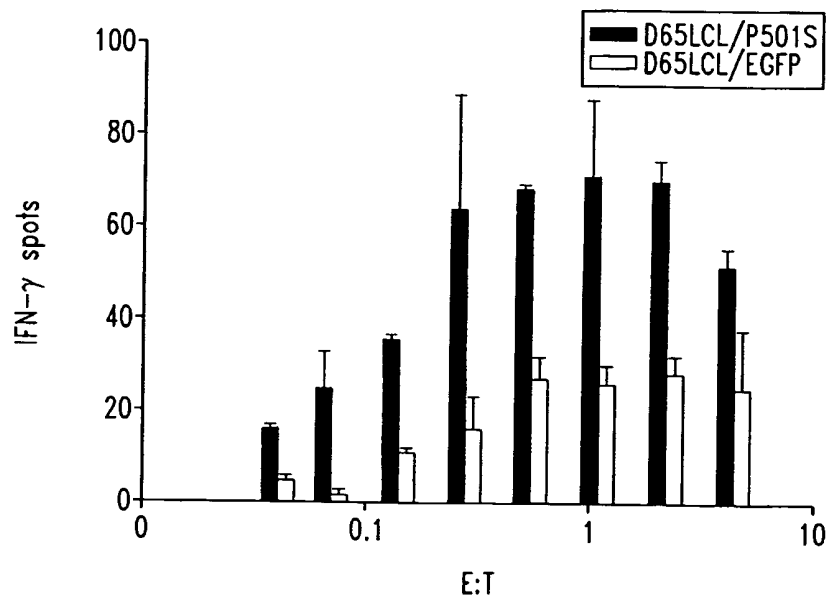
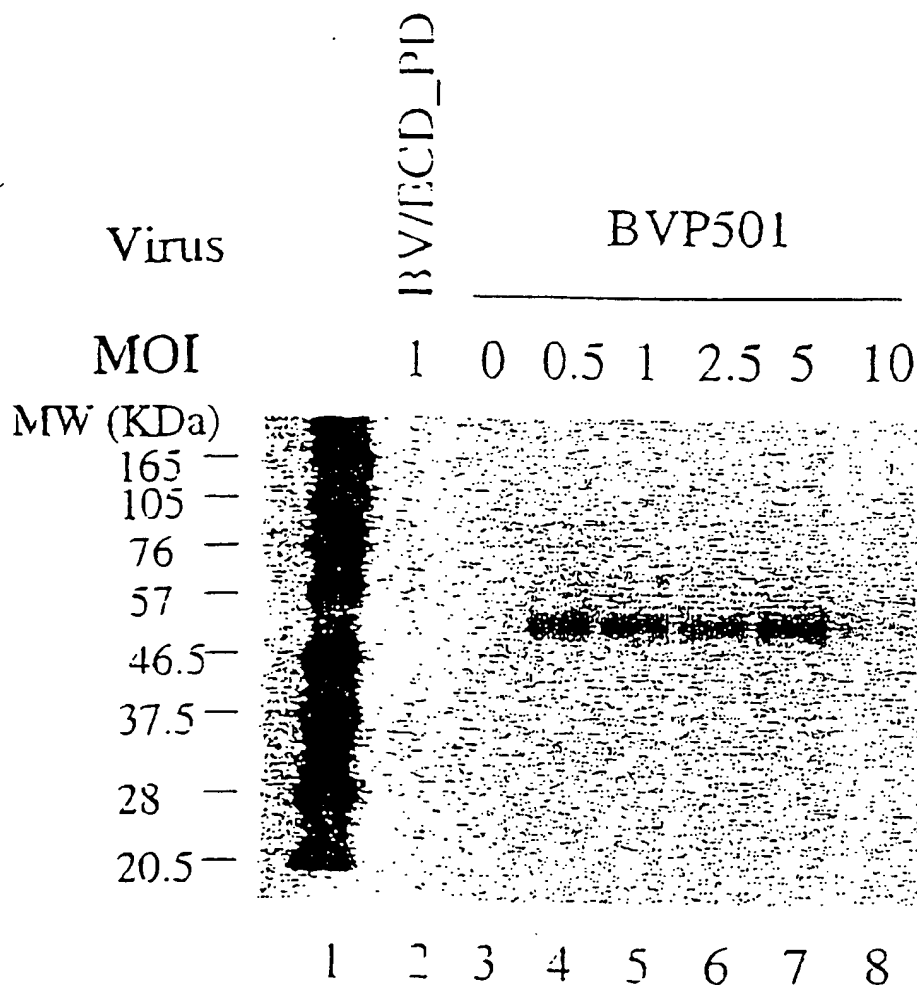


Fig. 3

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

# Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 – 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7



Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

MVQRLWVSRLLRHRK AQLLLVNLLTFGLEVCLAAGIT YVPPLLLEVGVEEKFM  
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 HQLCCRMPTLRR LFVAELCSWMALMTFTLFYTDF VGEGLYQGVPRAPGTEARRHYDEGVR  
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VTAYMVSAAGLGLVAIYFAT QVVFDKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:  
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

*Fig. 9*

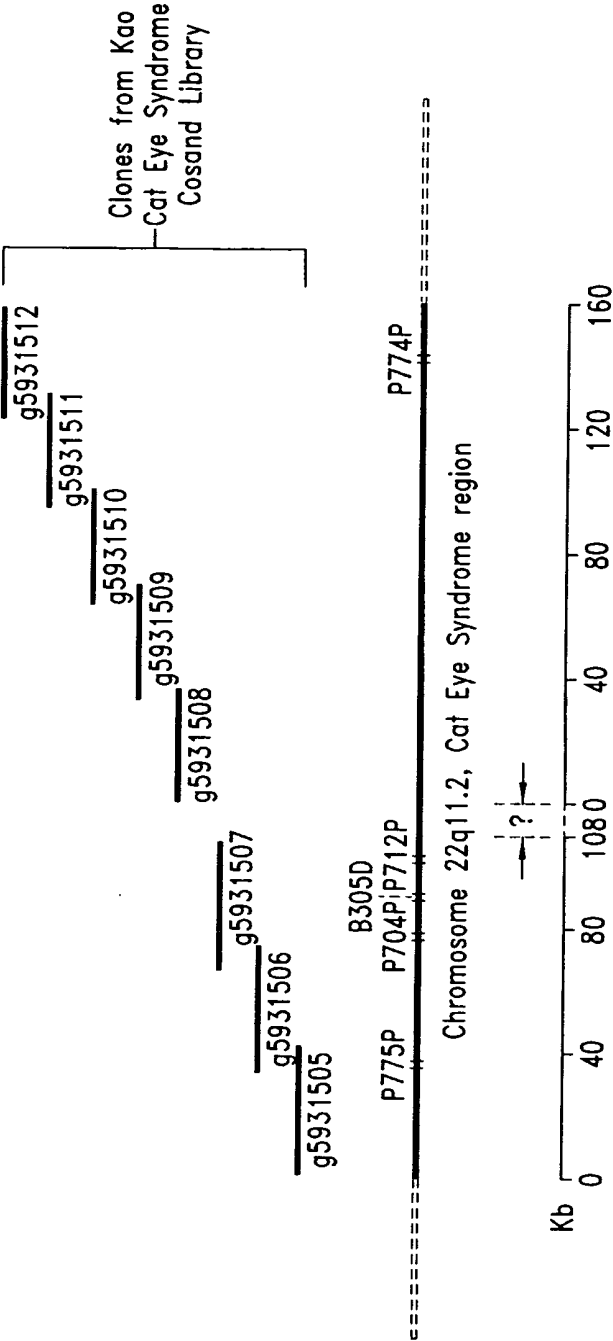


Fig. 10



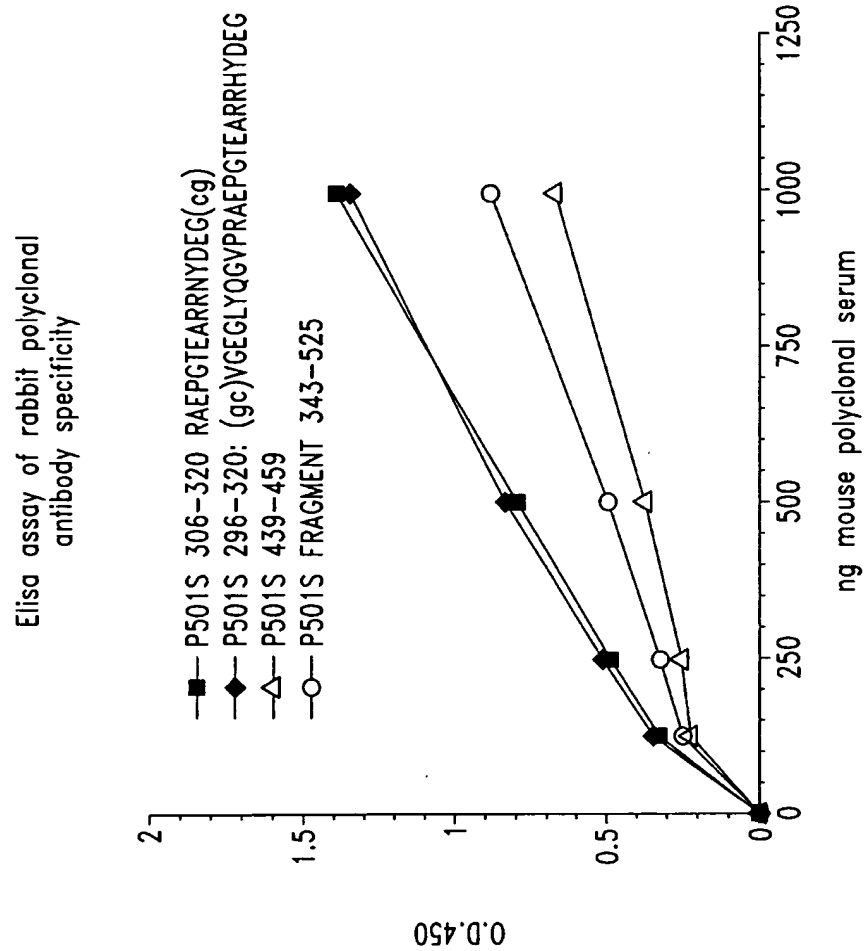


Fig. 11

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
 Harlocker, Susan Louise  
 Jiang Yuqui  
 Reed, Steven G.  
 Kalos, Michael  
 Fanger, Gary  
 Retter, Mark  
 Solk, John  
 Day, Craig  
 Skeiky, Yasir A.W.  
 Wang, Aijun

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND  
 DIAGNOSIS OF PROSTATE CANCER

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gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatggt	gagccgtaga	tgccgtcgga	240
aatggtgaag	ggagactcga	agtactctga	ggctttagtg	agggtaaaat	agagaccag	300

taaaattgta	ataagcagt	cttgaattat	ttggtttcg	ttgttttcta	ttagactatg	360
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ttantangg	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	ngggctctgg	ctnggtttta	cccnacccat	780
ggaatncnc	ccccggacna	ntgnatccct	attcttaa			818

&lt;210&gt; 7

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 7

tttttttttt	tttttttttt	tggtctctaga	gggggtagag	gggggtgctat	agggtaaata	60
cgggccctat	ttcaaagatt	tttaggggaa	ttaattctag	gacgatgggt	atgaaactgt	120
ggtttgcctc	acagatttca	gagcattgac	cgtagtatac	ccccggctcg	gtageggtga	180
aagtggtttg	gttttagacgt	ccgggaattg	catctgtttt	taagcctaata	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatgggggct	tcaatcggga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcaggctcgc	tggttcttagg	aataatgggg	360
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attggtggcc	aattgatttg	atggtaagg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
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tcaaacngtc	tctanttcct	gaaacgtctg	aaatgttaat	aanaattaan	tttngttatt	600
gaatnttng	gaaaagggtc	tacaggacta	gaaaccaaata	angaaaanta	atnntaang	660
cnttatctn	aaaggtnata	accnctccta	tnatcccacc	caatngnatt	ccccacncnn	720
acnattggat	nccccanttc	canaaaanggc	cnccccccg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	ccctngcntt	atcance			817

&lt;210&gt; 8

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

catttccggg	tttactttct	aaggaaagcc	gagcgggaagc	tgctaacgtg	ggaatcgggtg	60
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ctgaagcgca	cgteccagaa	ggtggacttg	gcactgaaac	agctgggaca	catccgcgag	180
tacgaacagc	gcctgaaagt	gctggagcgg	gaggtccagc	agtgtagccg	cgctcctggg	240
tgggtggccg	angcctganc	cgtctgcct	tgtgcccc	angtgggccc	ccaccccttg	300
acctgcctgg	gtccaaacac	tgagccctgc	tggcggactt	caagganaac	ccccacang	360
ggattttgct	cctanantaa	ggctcatctg	ggcctcggcc	ccccacctg	gttggccttg	420
tctttgagnt	gagccccatg	tccatctggg	ccactgtcng	gaccaccttt	ngggagtggt	480
ctccttacia	ccacannatg	ccgggtcct	cccgaaaacc	antcccance	tgngaaggat	540
caagnctgn	atccactnnt	nectanaaccg	gcncncnccg	cngtggaacc	cnccttntgt	600
tccttttct	tnagggttaa	tnnccgcttg	gccttnccan	ngtctcncnc	nttttccnnt	660

gttnaaattg ttangcnccc nccntcccn cnnnnnnan cccgaccenn annttnnann	720
ncctgggggt nccnnngat tgaccenncc nccctntant tgcnttnggg nncnntgccc	780
ctttccctct nggganncg	799

<210> 9  
 <211> 801  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (801)  
 <223> n = A,T,C or G

<400> 9	
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taangatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct	120
caaggacaag gccaccagggt gcgggggccg aagcccacat gatecttact ctatgagcaa	180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggaccang	240
caggtcatgg ggttgtnnc caactggggg ccncaacgca aaanggcna gggcctcngn	300
cacccatccc angacgcggc tacactnctg gacctccnc tccaccactt tcatgcgctg	360
ttcntaccgc cgnatntgtc ccantgttt cngtgcenac tccancttct nggacgtgcg	420
ctacatacgc cggantcnc nctcccgtt tgtccctatc cacgtnccan caacaaattt	480
cncntantg caccnatcc cacttttnc agntttcnc nncngcttc cttntaaaag	540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaaactn cccctnata	600
gctgaantcc ccatnaccnn gnctcnatgg anccntcnc ttttaannacn tctnaaactt	660
gggaanance ctcgnccntn ccccnttaa tccnccttg cnangnncnt ccccnntcc	720
nccnnntng gcntntnann cnaaaaagge ccnnnancaa tctcctnnen cctcanttgc	780
ccanccctcg aaatcgccn c	801

<210> 10  
 <211> 789  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (789)  
 <223> n = A,T,C or G

<400> 10	
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agatcctgcc ctacacactg gcctccctct accaccggga gaagcagggt ttctgtccca	180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc	240
caggccctaa gcctggagct cccttcccta atggacacgt ggggtgctgga ggcagtggcc	300
tgtcccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg	360
tggtgggtga gccaccgan gccaggggtg ttccggggcg gggcatctgc ctggacctgc	420
ccatcctgga tagtgcttcc tgetgtccca nggtggccca tccctgttta tgggtccat	480
tgtccagctc agccagtctg tcaactgccta tatggtgtct gccgcaggcc tgggtctggt	540
cccatttact ttgtacaca ggtantattt gacaagaacg anttgccaa atactcagcg	600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc	660
tcctgttaac cccatggggc tgccggcttg gccgccaatt tctgttgcctg ccaaantnat	720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng	780
gnggttccc	789

<210> 11  
 <211> 772

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (772)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 11

cccaccctac	ccaaatatta	gacaccaaca	cagaaaagct	agcaatggat	tcccttctac	60
tttgttaaat	aaataagtta	aatattttaa	tgctgtgtgc	tctgtgatgg	caacagaagg	120
accaacaggc	cacatcctga	taaaaggtaa	gaggggggtg	gatcagcaaa	aagacagtgc	180
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actttcata	gttcaaatac	catggaggag	tgtttcatcc	tagaaactcc	catgcaagag	300
ctacattaaa	cgaagctgca	ggttaagggg	cttanagatg	ggaaaccagg	tgactgagtt	360
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aactggggaa	aaaagaaaag	gacgccccan	ccccagctg	tgcanctacg	cacctcaaca	600
gcacaggggt	gcagcaaaaa	aaccacttta	ctttggcaca	aacaaaaact	ngggggggca	660
acccgggcac	cccnangggg	gttaacagga	ancngggnaa	cntggaaccc	aattnaggca	720
ggcccnccac	ccnaatntt	gctgggaaat	tttctctccc	ctaaatntt	tc	772

&lt;210&gt; 12

&lt;211&gt; 751

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (751)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 12

gcccccaattc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttggg	gcagggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
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atgggtgtgt	tccacacttg	agtgaagtct	tcttggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	ggaagtgtct	agccattgtg	gtgtacacca	aggcgaccac	360
agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
acacttgctc	tcagtcttan	caccatanca	gcccntgaaa	accaananca	aagaccacna	480
cnccggctgc	gatgaagaaa	tnaccccneg	ttgacaaact	tgcatggcac	tggganccac	540
agtggccnna	aaaatcttca	aaaaggatgc	cccactnatt	gaccccccaa	atgcccactg	600
ccaacagggg	ctgccccacn	cncnnaacga	tgancnatt	gnacaagatc	tncntggtct	660
tnatnaacnt	gaacctgcn	tngtggctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagncccca	cngganannc	g			751

&lt;210&gt; 13

&lt;211&gt; 729

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (729)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 13

gagccaggcg	tcctctgcc	tgccactca	gtggcaacac	ccgggagctg	ttttgtcctt	60
tgtggancct	cagcagtncc	ctctttcaga	actcantgcc	aaganccctg	aacaggagcc	120
accatgcagt	gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gctcatcttt	180
ctgtgtggtg	cagccctggt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatccttt	240
ctgaagatct	tcgggccact	gtcgtccagt	gccatgcagt	ttgtcaacgt	gggctacttc	300
ctcatcgcag	ccggcggttg	ggtcttagct	ctaggtttcc	tgggctgcta	tggtgctaag	360
actgagagca	agtgtgccct	cgtgacgttc	ttcttcatcc	tcctcctcat	cttcattgct	420
gagggttgcaa	tgtgtgtgtc	gccttggtgt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgtgtgtaat	gcctgccatc	aanaaaagat	tatgggttcc	caggaanact	tactcaagt	540
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gaagantcac	ctacttcaaa	gaaaaanagt	cctttccccc	atttctgttg	caattgacaa	660
acgtccccaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggtcc	ccaaccanaa	720
attnaaggg						729

&lt;210&gt; 14

&lt;211&gt; 816

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (816)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 14

tgtcttctct	caaagtgtgt	cttgttgcca	taacaaccac	cataggtaaa	gcgggagcag	60
tgctcgtga	aggggttgta	gtaccagcgc	gggatgctct	ccttgacagag	tcctgtgtct	120
ggcagggtcca	cgagtgccc	tttgtcactg	gggaaatgga	tgcgctggag	ctcgtcaaa	180
ccactcgtgt	atttttcaca	ggcagcctcg	tccgacgcgt	cggggcagtt	gggggtgtct	240
tcacactcca	ggaaactgtc	natgcagcag	ccattgctgc	agcggaactg	ggtgggctga	300
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tganncccan	anctgcctct	caaangcccc	accttgacac	ccccgacagg	ctagaatgga	420
atcttctctc	cgaaaggtag	ttnttcttgt	tgcccaancc	ancccentaa	acaaactctt	480
gcanatctgc	tccngggggg	tcnantacc	ancgtgggaa	aagaacccca	ggcngcgaa	540
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gggacaaggt	aantngccnt	cctttnaatt	cccnanctn	ccccctggtt	tggggttttn	720
cncnctccta	ccccagaaan	nccgtgttcc	cccccaacta	ggggccnaaa	ccnntnttcc	780
cacaaccctn	ccccaccac	gggttcngnt	ggttng			816

&lt;210&gt; 15

&lt;211&gt; 783

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (783)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 15

ccaaggcctg	ggcaggcata	nacttgaagg	tacaacccca	ggaacccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgcctactgc	ggggtgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcact	gtgctgtcca	240
ccaagcagac	agaagactac	tgcctcgcac	ccaacaangt	gggtcgtgc	cggggctctt	300
tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttcgtt	tatggaggct	360



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gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctance tgtcnggggtg 420
tgcaagggtg gcctttgana ngcanctctg gggctcangc gactttcccc cagggccct 480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccaccag ttccgctgca 540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgccccaa 600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg 660
cncctcctnt tccccnntn aacaaagggc nctngcnttt gaactgccc aaccnnggaa 720
ctcnccnngg aaaaantncc ccccttggtt cctnnaance cctcncnnaa anctncccc 780
ccc

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```

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (801)
<223> n = A,T,C or G

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```

<400> 16
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ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
aagtaggggt agtcctcaaa atccgtatag ttgggtgaagc cacagcactt gagccctttc 240
atgggtgtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtcga gccattgtgg tgtacacca ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
ccngctgcga atgaaagaaa ntaccacgt tgacaaactg catggccact ggacgacagt 540
tgccccgaan atcttcagaa naaggatgcc ccatcgattg aacacccana tgccactgc 600
cnacagggct gncncncn gaaagaatga gccattgaag aaggatcntc ntgggtcttaa 660
tgaactgaaa cntgcatgg tggccctgt tcagggtctt tggcagtga ttctganaaa 720
aaggaacngc ntnagcccc ccaaangana aaacaccccc ggggtgttgc ctgaattggc 780
ggccaaggan ccctgccccn g
801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (740)
<223> n = A,T,C or G

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```

<400> 17
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cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgttca gtttcattaa gaccatgatg atcctcttca atttgctcat 180
ctttctgtgt ggtgcagcc tgttggcagt gggcatctgt gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300
cttctctatc gcagccggcg ttgtggctct tgccttgggt ttccctgggt gctatgggtc 360
taagacggag agcaagtgtg cctcgtgac gttctctctc atcctcctcc tcatcttcat 420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct 480
gacgttctg gtantgctg ccatcaanaa agattatggg tcccaggaa aaattcactc 540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg 600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcccttncc ccnttctgt 660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa 720

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caaaaaaant nnaagggttn

740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1) ... (802)  
 <223> n = A,T,C or G

<400> 18  
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 ggatacactt tacttttagca gccagggtag caactgagag gtgtcgaagc ttattcttct 180  
 gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240  
 aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300  
 cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360  
 ggatgagtgt ggccagcgtt gccccttgg ccgacttggc taggagcaga aattgctcct 420  
 ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480  
 gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc 540  
 gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cinctacttgc 600  
 aancttcgtc nggccatgg aattcacnc accggaactn gtangatcca ctnttctat 660  
 aaccggnccg caccgcnnt ggaactccac tcttnttnc tttacttgag ggtaagggtc 720  
 acccttnnccg ttaccttggg ccaaaccntn cntgtgtcg anatngtnaa tcnggncena 780  
 tnccancnc atangaagcc ng 802

<210> 19  
 <211> 731  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (731)  
 <223> n = A,T,C or G

<400> 19  
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 gagcccaccg tcacngngng gngtctttat nggagggggc ggagccacat cnetggacnt 120  
 cntgacccca actcccnc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180  
 caggaacca gancaaannc tgctccnntc caagtcggcn nagggggcgg ggctggccac 240  
 gncatccnt cnagtgtgn aaagccccnn cctgtctact tgtttgaga acngcnnga 300  
 catgcccagn gttanataac nggcnagag tnannttgcc tctcccttcc ggctgcgan 360  
 cgngtntgct tagnggacat aacctgacta cttaactgaa ccnngaate tnccnccct 420  
 ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480  
 aagtgtacc catnccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg 540  
 gaagacctat caattnaagc tatgtttctg actgctctt gctccctgna acaancnacc 600  
 cncnntcca agggggggnc ggcccccaat ccccccaacc ntnaattnan ttancccn 660  
 ccccnnggc cggcctttta cnancntenn nnacngggna aaaccnnngc ttncccaac 720  
 nnaatcncc t 731

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 ,tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caacccctc ntccaaatnn ccntttccgg gnggggggtc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagt naaccanta 180  
 tnancttnaa tncctgaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240  
 aaatngttna nggaaaaccc aanttctcnt aaggttggtt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360  
 gggnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntccggg 480  
 ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540  
 ccaggntgag nntnggggtt ncccccccc cangggccct ctcgnanagt tgggggtttg 600  
 ggggcctggg attttnttcc cctntttccc tcccccccc ccnggganag aggttngngt 660  
 tttgntcncn ggccccnccn aaganctttn ccganttnan ttaaatecnt gcctnggcga 720  
 agtccttgn agggntaaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
 atcancccat gacccnaac nngggaccnc tcanccggnc nnncnaccnc cggccnatca 60  
 nngtnagnnc actncnnttn natcacnccc cnccnactac gcccncnanc cnacgcncta 120  
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacnng nnnatccaat ntgnancctc cnaagtattn 240  
 nncnncanat gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300  
 cgaaggcnct ggncnnaagg nngcgnccnc ccgctagntc ccnncnaagt cncnncncta 360  
 aactcancn nattacnccg ttcttgagta tcactcccc aatctcacc tactcaactc 420  
 aaaaanactn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnggtcc ntnaanctc ctaatacttc cagtctncc tcnccaattt ccnaanggt 540  
 ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttctntgaac 600  
 gggctcntct tttccttcgg ttancctggg ttcnncggc cagttattat ttccntttt 660  
 aaattcntnc cntttanttt tggcnttcna aacccccggc cttgaaaacg gccccctggt 720  
 aaaaggttgt tttganaaaa tttttgtttt gtccc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)  
 <223> n = A,T,C or G

<400> 22  
 tttttttttt tttttangtg tngtctgtca ggtagaggct tactacaant gtgaanacgt 60  
 acgctnggan taangcgacc cgantttctag gannccctt aaaatcanac tgtgaagatn 120

```

atcctgnnna cggaanggtc accggnngat nntgctaggg tgnccnetec cannnenttn 180
cataactcng nggcctgcc caccaccttc ggcgccceng ngncgggcec cgggtcattn 240
gnnttaaccn cactnngcna ncggtttccn nccccnneng acccnggcga tccgggggtnc 300
tctgtcttcc cctgnagncn anaaantggg ccncggnecc ctttaccct nnacaagcca 360
cngcctcta nccnngccc cccctccant nngggggact gccnannget ccgttntctng 420
nnaccccnnn gggtnccctg gttgtcgant cnaccgnang ccanggattc cnaaggaagg 480
tgcgttnttg gcccctaccc ttcgctnccg nncacccttc ccgacnanga nccgctcccg 540
cncnncgnng cctcncctcg caacacccgc nctcntengt ncggnnnccc cccacccgc 600
nccctcncnc ngncgnancn ctccnccncc gtctcannca ccaccccgcc ccgccaggcc 660
ntcanccaen ggngacnng nagnccnttc gcncgcgcgn gcgncnccct cgcncngaa 720
ctnctcngg ccantnccg tcaancnna cnaaacgcg ctgcgcggcc cgnagcgncc 780
ncctcncga gtcctccgn ctccnacc angnttccn cgaggacacn nnaccccgcc 840
nncangcgg 849

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&lt;210&gt; 23

&lt;211&gt; 872

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(872)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 23

```

gcgcaaaacta tactcgctc gnactcgtgc gcctcgtcnc tcttttcttc cgcaaccatg 60
tctgacnanc cegattnggc ngatatchan aagntcganc agtccaaact gantaacaca 120
cacacnncan aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc 180
nggcgaatcg taatnaggcg tgcgcgcca atntgtcncc gtttatntn ccagctcnc 240
ctnccnacc taactcttcn nagctgtcnn acccctngtn cgnaccccc naggtcggga 300
tcgggtttnn nntgaccgng cnnccctcc cccctccat nacganccnc ccgcaccacc 360
nanngcncgc nccccgnct ctctgcncncc ctgtcctntn cccctgtngc ctggcncngn 420
accgcattga cctcgcenn ctncnngaaa ncgnanacgt ccgggttggn annancgctg 480
tgggnngcg tctgcncgc gttccttcn ncnncttcca ccatcttct taengggct 540
cncgcctc tcnncacnc cctgggacgc tntcctntgc ccccttnac tccccctt 600
cgcgtgnc cgnccccacc ntcatttnca nacgntcttc acaannccet ggntnnctcc 660
cnancngn gtcancnag ggaagggng ggnnccnntg nttgacgtg ngngangtc 720
cgaanantcc tcnccntcan cctaccct cgggcgnct ctngttnc aacttanca 780
ntctcccc ngngcncntc tcagctcnc cncccnct ctctgcantg tnetctgctc 840
tnaccnntac gantnttcn cncctctt cc 872

```

&lt;210&gt; 24

&lt;211&gt; 815

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(815)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 24

```

gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggtcnta 60
nctgncttcc tgtgtcaaat gtatacnaa tanatatgaa tctnatntga caaganngt 120
tctnccatta gtaacaantg tntgtccat cctgtcngan canattccca tnnattncgn 180
cgcattcncn gncantatn taatngggaa ntcnnntnnn ncaccnncat ctatctncc 240
gcncctgac tggagagat ggatnanttc tntntgacc nacatgttca tcttgattn 300
aanaccccc cgcngnccac cggttngng cnagcnnct ccaagacctc ctgtggagg 360

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aacctgcgtc	aganncatca	aacntgggaa	accgcgncc	angtnnaagt	ngnnncanan	420
gatcccgctc	aggnttnacc	atcccttcnc	agcgccecc	ttngtgcctt	anagngnagc	480
gtgtccnanc	cntcaacat	ganacgcgcc	agnccanceg	caattnggca	caatgtcgnc	540
gaaccccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
ccnccctac	ccncttttg	gacngtgacc	aantcccga	gtncagtc	ggccngnctc	660
ccccaccggt	nncntgggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggnccctn	ggncgaann	ancnntcnga	agngccnct	cgtataaccc	cccctcncca	780
nccnacngnt	agntcccccc	cngggtnccg	aangg			815

<210> 25  
 <211> 775  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(775)  
 <223> n = A,T,C or G

<400> 25						
ccgagatgtc	tcgctccgtg	gccttagctg	tgtctgcgtc	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaat	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgtct	ttcagcaagg	240
actggtcttt	ctatctcntg	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300
cctgccgtgt	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcntttta	antgatatgc	ntatacaccc	taccctttat	gnccccaat	480
tgtagggtt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cncccngttn	ngaattgttc	cnnaaccacg	gttggtctcc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnctttncaa	gggtggggga	accnaaaatt	tcnctnttgc	660
ccncccncca	cnntcttgng	nncncanttt	ggaacccttc	cnattcccct	tggcctcnna	720
nccttnncta	anaaaacttn	aaancgtngc	naaanntttn	acttcccccc	ttacc	775

<210> 26  
 <211> 820  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(820)  
 <223> n = A,T,C or G

<400> 26						
anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatanca	acagtgtctt	gaccaagagc	tgtctgggcac	atttcctgca	120
gaaaagggtg	cgggtcccat	cactctctct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcgggtggga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgcttc	aagtgcaccc	360
ttctacctg	acnaccagn	accnnnaact	gcngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggcgg	tnccgntccc	tggctctgnc	aagggaagct	480
ccctgttgga	attncggggga	naccaaggga	nccccctct	ccanctgtga	aggaaaaann	540
gatggaattt	tncccttccg	gcnntcccc	tcttctttta	cacgccccct	nntactctnc	600
tcctctntt	ntcctgncnc	acttttnacc	ccnnnatttc	ccttnattga	tcggannctn	660
ganattgccac	tnncgectnc	cntcnatcng	naanacnaaa	nactntctna	ccnnggggat	720
gggnccctcg	ntcactctct	ctttttcnct	accnccnntt	ctttgctct	ccttngatca	780

tccaacntc gntggcctn ccccccnntc tccttttccc

820

<210> 27

<211> 818

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (818)

<223> n = A,T,C or G

<400> 27

tctgggtgat	ggcctcttcc	tcctcaggga	cctctgactg	ctctgggcca	aagaatctct	60
tgtttcttct	ccgagcccca	ggcagcgggtg	attcagccct	gcccacctg	attctgatga	120
ctgcggatgc	tgtgacggac	ccaaggggca	aatagggtcc	cagggtccag	ggaggggccc	180
ctgctgagca	cttcgcgcc	tcaccctgcc	cagccctgc	catgagctct	gggctgggtc	240
tcgcctcca	gggttctgct	cttcangca	ngccancaag	tggcgctggg	ccacactggc	300
ttcttctgc	ccctccctg	gctctganc	tctgtcttc	tgtctgtgc	angcnccttg	360
gatctcagtt	tcctcncctc	anngaactct	gttctgann	tcttcantta	actntgantt	420
tatnaccnan	tggnetgtnc	tgtcnaactt	taatgggccn	gaccggctaa	tcctccctc	480
netcccttcc	anttcnnna	acngcttnc	cncctctcc	ccntancccg	ccngggaanc	540
ctcctttgcc	ctnaccangg	gccnnnaccg	cccnnnctn	ggggggcngg	gtnnctncnc	600
ctgntnnccc	cncctcncnt	tncctcgtcc	cnnncncgn	nngcannttc	ncngtcccn	660
tnnctcttcn	ngntcgnaa	ngntcncntn	tnnnnngncn	ngntnntncn	tcctctcnc	720
cnnntgnang	tnnttnnnnc	ncngnncccc	nnnnnnnnnn	nggnnnntnn	tctnncngc	780
ccnncccccc	ngnattaagg	cctcncntct	ccggccnc			818

<210> 28

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (731)

<223> n = A,T,C or G

<400> 28

aggaagggcg	gagggatatt	gtangggatt	gagggatagg	agnataangg	gggaggtgtg	60
tcccaacatg	anggtgnngt	tctcttttga	angaggggtg	ngtttttann	ccnggtgggt	120
gattnaaccc	cattgtatgg	agnnaaaggn	tttnagggat	ttttcggtc	ttatcagtat	180
ntanattcct	gtnaatcgga	aaatnatntt	tcnnncggaa	aatnttgctc	ccatccgnaa	240
attncctccg	ggtagtgcac	nttngggggg	cngccangtt	tcccaggctg	ctanaatcgt	300
actaaagntt	naagtgggan	tncaaagtaa	aacctnncac	agagnatccn	taccgcactg	360
tnnnttncct	tcgccctntg	actctgcnn	agcccaatac	ccnnngnngnat	gtcncncngn	420
nnngcgnenc	tgaaannnn	tcgnggctnn	gancatcang	gggtttcgca	tcaaaagcnn	480
cgtttcncat	naaggcactt	tngcctcacc	caaccncctg	ccctcnncca	tttngccgtc	540
nggttcncct	acgctnntng	cncctnnntn	ganattttnc	ccgcctnggg	naancctcct	600
gnaatgggta	gggncttntc	ttttnacnnc	gnggtntact	aatcnnctnc	acgctnctt	660
tctcnacccc	cccccttttt	caatcccanc	ggcnaatggg	gtctcccenn	cgangggggg	720
nnnccannnc	c					731

<210> 29

<211> 822

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (822)  
 <223> n = A,T,C or G

<400> 29  
 actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat 60  
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120  
 atntntacnc tcatannect cnnaaccac tccctcttaa ccctactgt gcctatngcn 180  
 tnntantct ntgcgcctn cnanccaccn gtgggcnac cncnngnatt ctcnatctcc 240  
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300  
 tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc 360  
 tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaadc 420  
 ntcaacaacc tatctantct ttncceaacc nttncctcgc atcccccnac aacccccctc 480  
 ccaaataccc nccactgac ncctaaccen caccatcccg gcaagccnan ggcatttan 540  
 ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600  
 aatnctectn naatttactn ncantnccat caanccacn tgaaacnaa cccctgtttt 660  
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc cccccnctnc 720  
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780  
 canatcctat cccttanttn ggggnccctt nccngggcc cc 822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (787)  
 <223> n = A,T,C or G

<400> 30  
 cggccgcctg ctctggcaca tgccctcctga atggcatcaa aagtgatgga ctgcccattg 60  
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120  
 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna 180  
 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccacg ctctccangg 240  
 acaccagggg ctccaggcag cccattatct ccagnangac atgggtgtttc tccacgcgga 300  
 cccatggggc ctgnaaggcc aggggtctct ttgacaccat ctctcccgtc ctgcctggca 360  
 ggccgtggga tccactantt ctanaacggn cgcaccncg gtgggagctc cagcttttgt 420  
 tccnttaat gaagggtaat tgcnegcttg gcgtaatcat nggtcanaac tntttcctgt 480  
 gtgaaattgt ttntccccctc ncnatccnc ncnacatacn aacccggaan cataaagtgt 540  
 taaagcctgg gggtngectn nngaataaac tnaactcaat taattgcgtt ggctcatggc 600  
 cegctttccn ttenggaaaa ctgtentccc ctgenttntt gaatcggccca cccccnggg 660  
 aaaagcggtt tgcnttttng ggggntcctt ccncttcccc cctcnctaan cccnccgct 720  
 cggtcgttnc nggtngcggg gaangggnat nnnctcccnc naagggggng agnnngntat 780  
 ccccaaa 787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (799)  
 <223> n = A,T,C or G

<400> 31

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tttttttttt tttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac      60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc      120
aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct      180
cccgcagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg      240
gtggctggtg cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca      300
ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt      360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca      420
tatggttcg gcccacctct cccntcnaa aagtaattca ccccccccn cntctnttg      480
cctgggcccet taantacca caccggaact canttantta ttcactctng gntgggcttg      540
ntnatcnccn cctgaangcg ccaagttgaa aggccacgcc gtncnccnctc cccatagnan      600
nttttnnct canctaagtc cccccnggc aacnatccaa tcccccccn tgggggcccc      660
agcccanggc ccccgntctg ggnnnccngn cncgnantcc ccaggntctc ccantcngnc      720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnncnac      780
ctcgcccccc ccnncgnng

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<210> 32

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(789)

<223> n = A,T,C or G

<400> 32

```

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac      120
ggcaacaggc tccggcggcg gcggcggcgg cctacctgc ggtaccaa atgtcagcctc      180
cgctcccget tgatnttctt ctgcagctgc aggatgccnt aaaacagggc ctcggccntn      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc      300
nattaggaat agtggnttta ccnccnccg ttggcncact cccntggaa accacttntc      360
gcggctccgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt      420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc      480
ggnccatgtc ttnnccgggt tgctgcnatn tncatcacct cccgggcncn ncaggncaac      540
ccaaaagttc ttgnggccc caaaaaanct ccgggggggnc ccagtttcaa caaagtcac      600
ccccttggcc cccaaatcct ccccccgnt nctgggtttg ggaacccacg cctctnnctt      660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnctctaa ngaaaaacnc      720
ntcctnnnca ccaccccc nngnnacgnc tancaangna tccctttttt tanaaacggg      780
ccccccncc

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<210> 33

<211> 793

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(793)

<223> n = A,T,C or G

<400> 33

```

gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgac aaaggacttg      120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana      180
agaagtttgc agatgtatth gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg      240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttggtcat catgatcaca      300
acaangaacg gggctcgtht atcaccantg aggagcagga cgtgagcccc cgcctgcac      360

```



```

ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaatc atgggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaaattht aaagcctggg ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgcttttc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncttccc gctttctcgc ttctctgaant ccttcccccc ggtctttcgg cttgcggcna 780
acggtatcna cct 793

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```

<210> 34
<211> 756
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (756)
<223> n = A,T,C or G

```

```

<400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag ccccaatctt 60
ancaagtgcg gggaanagct gggtcgactc aagctagttht ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtag catactggag 180
atcgggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaa gtnttcttg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc ttttctctga aggccccgg 600
atnctnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttncctt 660
ttactgaggg ttnattgccg cctttggcgt tatcatgggt acnccngttn cctgtgttga 720
aattnttaac cccccacaat tccacgcena cattnng 756

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<210> 35
<211> 834
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (834)
<223> n = A,T,C or G

```

```

<400> 35
ggggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgcgtgc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggtt gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cnetcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcnng gctgtctgct cgggtgaact gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctcct tggtagcttc ccttcaaaag ttgttcggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactggt 360
ggaaactgat cccaaatggg atgtcatcca tcgctctgc tgcttgcaaa aaacttgctt 420
ggcncaaatc cgactcccn tcttgaaag aagccnatca cccccctc cctggactcc 480
nncaangact ctncgcctnc cccntccnng cagggttggg ggcanncgg gccntgcgc 540
ttcttcagcc agttcacnat ntcatcagc cctctgccg gctgtnttat tcttggggg 600
ggaanccgct tctccttcc tgaannaact ttgacctng gaatagccgc gcntcncnt 660
acntnctggg cgggttcaa antcctccn ttgcnntcn cctcgggcca ttctggattt 720
nccnaacttt tctcttcccc cncnccnng ngtttggntt tttcatnggg ccccaactct 780

```

gctnttggcc antcccttgg gggcntntan cnccttnt ggtccctng ggcc 834

<210> 36  
 <211> 814  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(814)  
 <223> n = A,T,C or G

<400> 36  
 cggncgcttt ccngccgcgc ccggtttcca tgacnaaggc tcccttcang ttaaatacnn 60  
 cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcca 120  
 naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggctctctc acccctgta 180  
 ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240  
 aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca 300  
 ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgcctt ttggacatca 360  
 ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420  
 antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480  
 aggggangtc ntttncagtg gatctgcaa anantaccen tatcatcnnt gaataaaaag 540  
 gcccctgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatgggtgcc 600  
 cttccggtct gatccnaaag gaatgttctt ggggtccant ccctccttg ttncctacgt 660  
 tgtnttggac cctgtctnng atnaccctaan tganatcccc ngaagcacc tncctctggc 720  
 atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnnaan 780  
 ggngaactca agaaggtctn ngaaaaacca cncn 814

<210> 37  
 <211> 760  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(760)  
 <223> n = A,T,C or G

<400> 37  
 gcatgtgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60  
 gcgcagtgtt cgctgaagg gttgtagtac cagcgcgga tgctctcctt gcagagtcct 120  
 gtgtctggca ggtccacgca atgcccttg tcactgggga aatggatgcy ctggagctcg 180  
 tcnaanccac tcgtgtattt ttcacangca gcctcctccg aagcttccgg gcagttgggg 240  
 gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300  
 gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat 360  
 cncctnancc caaactgcct ctcaaaggcc acctgcaca ccccgacagg ctagaaatgc 420  
 actcttcttc ccaaaggtag ttgttcttg tgcccaagca ncctccanca aaccaaanc 480  
 ttgcaaaatc tgctcgtgg gggatcatnnn taccanggtt ggggaaanaa acccgcnngn 540  
 ganccnctt gtttgaatgc naaggaata atcctcctgt cttgcttggg tggaanagca 600  
 caattgaact gttaacnttg ggccgngtcc cncnnggtg gtctgaaact aatcacgctc 660  
 actggaaaaa ggtangtgc ttccttgaat tcccaantt cccctngntt tgggtntttt 720  
 ctctctncc ctaaaaatcg tnttcccccc centanggcg 760

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38  
 tttttttttt tttttttttt tttttttttt ttttttaaaa cccctcccat tgaatgaaaa 60  
 cttccnaaat tgtccaaccc cctcnccaa atnnccattt ccgggggggg gttccaaacc 120  
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
 aatttaaccc attatnaact taaatncctn gaaacccttg gnttccaaaa atttttaacc 240  
 cttaaattcc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300  
 ngatttaaac ccccttnant tnttttnacc cnnngctnaa ntatttngnt tccggtgttt 360  
 tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt 420  
 tttttgaatt ggaaattccn ngggaattna ccgggggttt tcccntttgg gggccatncc 480  
 cccnctttcg ggggttgggn ntaggttgaa ttttttnang ncccaaaaaa ncccccaana 540  
 aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttgg gaaaggnggg 600  
 tttntggggg ccngggantt cnttcccccn ttncncccc cccccnggt aaanggttat 660  
 ngnntttggt ttttgggccc cttnanggac ctccggatn gaaattaaat ccccggnncg 720  
 gccg 724

<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 39  
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120  
 tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180  
 ggccgcctta agctttctaa atttggaaca tetaagcaag ctgaanggaa aagggggttt 240  
 cgcaaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
 ttaactgctt gtacaattac ntttactttt taattaattg tgctnaangc ttttaattana 360  
 cttgggggtt ccttccccan accaaccctn ctgacaaaaa gtgccngccc tcaaatnatg 420  
 tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa 480  
 tgaagggtta ccatntttta cncacctcc acntggcnnn gcctgaatcc tcnaaaancn 540  
 cctcaancn aattnctnng ccccggtcnc gentnngtcc cncccgggct ccgggaantn 600  
 cacccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
 cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgnnc cnnaaatgn 720  
 nnnncctc cncnngtcen naatcnccan c 751

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)  
 <223> n = A,T,C or G

<400> 40  
 gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat 60  
 agatgaaaac ccccccgaga cagcagcact gcaactgcc aagcagccgg gtaggagggg 120

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cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa 180
tggctctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact 240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccagggtgatn agcttgggggt 300
cggtcataaan cgcgggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna 360
ataaaagggtg cgccccgca ccgttcantc cgcacttctc naanaccatg angttgggct 420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gccctanctg gttgccnngn atgccaanca nccccaancc ccggggctcct 540
aaanaccn cctcctcntt tcctctgggt tntntcccc ggacctgggt tcctctcaag 600
ggancccata tctcnaccan tactcacnt nccccccnt gnnaccanc cttctanngn 660
ttccncccg ncctctggcc cntcaaanan gcttnacna cctgggtctg ccttcccccc 720
tnccctatct gnaccnccn tttgtctcan tnt 753

```

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<210> 41
<211> 341
<212> DNA
<213> Homo sapien

```

```

<400> 41
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaagt 60
agtgaaccaca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt 180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttag 240
tgtaaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300
ttttactttt tgattaattg tgttttatat attagggtag t 341

```

```

<210> 42
<211> 101
<212> DNA
<213> Homo sapien

```

```

<400> 42
acttactgaa tttagttctg tgctcttctt tatttagtgt tgtatcataa atactttgat 60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

```

```

<210> 43
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 43
acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttcctg gtcctcacc 60
tccaggggtg tctcactg taattagagc tattgaggag tctttacagc aaattaagat 120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca 180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cgggggcccgc 300
tcgaa 305

```

```

<210> 44
<211> 852
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (852)
<223> n = A,T,C or G

```

```

<400> 44

```

acataaatat	cagagaaaag	tagtctttga	aatatattacg	tccaggaggt	ctttgtttct	60
gattatttgg	tgtgtgtttt	ggtttgtgtc	caaagtattg	gcagcttcag	ttttcatttt	120
ctctccatcc	tggggcattc	ttcccaaatt	tatataccag	tcttcgtcca	tccacacgct	180
ccagaatttc	tctttttag	taatatctca	tagctcggct	gagcttttca	taggtcatgc	240
tgtgtgtgtt	cttcttttta	ccccatagct	gagccactgc	ctctgatttc	aagaacctga	300
agacgccctc	agatcggctc	tcccatttta	ttaatcctgg	gttcttgtct	gggttcaaga	360
ggatgtcgcg	gatgaattcc	cataagttag	tccctctcgg	gttgtgcttt	ttgggtgtgc	420
acttggcagg	ggggctctgc	tcctttttca	tatcagggtga	ctctgcaaca	ggaaggtgac	480
tgggtggtgt	catggagatc	tgagcccggc	agaaagtttt	gctgtccaac	aaatctactg	540
tgctaccata	gttgggtgtc	tataaatagt	tctngtcttt	ccagggtgtc	atgatggaag	600
gctcagtttg	ttcagtcttg	acaatgacat	tgtgtgtgga	ctggaacagg	tcactactgc	660
actggccggt	ccacttcaga	tgctgcaagt	tgctgtagag	gagntgcccc	gccgtccctg	720
ccgcccgggt	gaactcctgc	aaactcatgc	tgcaaagggt	ctcgccgttg	atgtcgaaact	780
cntggaaaag	gatacaattg	gcattccagct	ggttgggtgc	caggaggtga	tggagccact	840
cccacacctg	gt					852

<210> 45  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

acaacagacc	cttgctcgct	aacgacctca	tgctcatcaa	gttggacgaa	tccgtgtccg	60
agtctgacac	catccggagc	atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	120
gcctcgtttc	tggctggggg	ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	180
tgaacgtgtc	ggtggtgtct	gaggaggtct	gcagtaagct	ctatgaccgc	ctgt	234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (590)  
 <223> n = A,T,C or G

actttttatt	taaatgttta	taaggcagat	ctatgagaat	gatagaaaac	atggtgtgta	60
atttgatagc	aatatatttg	agattacaga	gttttagtaa	ttaccaatta	cacagttaaa	120
aagaagataa	tatatcccaa	gcanatacaa	aatatctaat	gaaagatcaa	ggcaggaaaa	180
tgantataac	taattgacaa	tggaaaatca	attttaatgt	gaattgcaca	ttatccttta	240
aaagctttca	aaanaanaa	ttattgcagt	ctanttaatt	caaacagtgt	taaattggat	300
caggataaan	aactgaaggg	canaaaagaat	taattttcac	ttcatgtaac	ncacccanat	360
ttacaatggc	ttaaatgcan	ggaaaaagca	gtggaagtag	ggaagtantc	aaggctcttc	420
tggctctctaa	tctgccttac	tctttgggtg	tggctttgat	cctctggaga	cagctgccag	480
ggctcctgtt	atatccacaa	tcccagcagc	aagatgaagg	gatgaaaaag	gacacatgct	540
gccttccttt	gaggagactt	catctcactg	gccaacactc	agtcacatgt		590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (774)  
 <223> n = A,T,C or G

```

<400> 47
acaagggggc ataatgaagg agtggggana gatttttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacggggcctt caaaataatt ttcttgggga ggttcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactctgg gaggaaggat aaacagaaaag gggacaaaag ctaatcccaa      240
aacatcaaag aaaggaaggt ggcgtcatat ctcccagcct acacagttct ccagggtctct      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg      360
ctggctcctg gtcttcagcc cccagctctg gaagccacc ctctgctgat cctgcgtggc      420
ccacactcct tgaacacaca tcccaggtt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgctg attactccag catcttgga caatccctga      600
ttccccactc cttagaggca agataggggt gttaagagta gggctggacc acttgagacc      660
aggtgtctgg cttcaaattn tggtcattt acgagctatg ggaccttggg caagtnatct      720
tcactttctat gggcntcatt ttgttctacc tgcaaatgg gggataataa tagt          774

<210> 48
<211> 124
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

<400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                              124

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

<400> 49
gccgatgcta ctattttatt gcaggagggtg ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                      147

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

<400> 50
acattaaatt aataaaagga ctgttgggggt tctgctaaaa cacatggctt gatatatattgc      60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt                      107

<210> 51
<211> 204
<212> DNA

```

<213> Homo sapien

<400> 51

gtcctaggaa	gtctagggga	cacacgactc	tgggggtcacg	gggccgacac	acttgacagg	60
cggaagga	aggcagagaa	gtgacaccgt	cagggggaaa	tgacagaaag	gaaaaatcaag	120
gccttgcaag	gtcagaaaagg	ggactcaggg	cttccaccac	agccctgccc	cacttgacca	180
cctccctttt	gggaccagca	atgt				204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (491)

<223> n = A,T,C or G

<400> 52

acaagataa	catttatctt	ataacaaaaa	tttgatagtt	ttaaagggtta	gtatttgtga	60
gggtattttc	caaaagacta	aagagataac	tcaggtaaaa	agttagaaat	gtataaaaca	120
ccatcagaca	ggttttttaa	aaacaacata	ttacaaaatt	agacaatcat	ccttaaaaaa	180
aaaacttctt	gtatcaattt	cttttgttca	aaatgactga	cttaantatt	tttaaatatt	240
tcanaaacac	ttcctcaaaa	attttcaana	tggtagcttt	canatgtnc	ctcagtccca	300
atgttgctca	gataaataaa	tctcgtgaga	acttaccacc	caccacaagc	tttctggggc	360
atgcaacagt	gtcttttctt	tnctttttct	tttttttttt	ttacaggcac	agaaactcat	420
caattttatt	tggataacaa	aggggtctcca	aatttatattg	aaaaataaat	ccaagttaat	480
atcactcttg	t					491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (484)

<223> n = A,T,C or G

<400> 53

acataattta	gcagggctaa	ttaccataag	atgctattta	ttaanaggtn	tatgatctga	60
gtattaacag	ttgctgaagt	ttggattttt	tatgcagcat	tttctttttg	ctttgataac	120
actacagaac	cettaaggac	actgaaaatt	agtaagttaa	gttcagaaac	attagctgct	180
caatcaaatc	tctacataac	actatagtaa	ttaaaacggt	aaaaaaaaag	gttgaaatct	240
gcactagtat	anaccgctcc	tgtcaggata	anactgcttt	ggaacagaaa	gggaaaaanc	300
agctttgant	ttctttgtgc	tgatangagg	aaaggctgaa	ttaccttggt	gcctctccct	360
aatgattggc	aggtcnggta	aatnccaaaa	catattccaa	ctcaacactt	cttttccncg	420
tancttgant	ctgtgtattc	caggancagg	cggatggaat	gggccagccc	ncggatgttc	480
cant						484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc	gtgcttgatga	actccataca	gaaaacgggtg	ccatccctga	acacggctgg	60
ccactgggta	tactgctgac	aaccgcaaca	acaaaaacac	aaatccttgg	cactggctag	120

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55  
 <211> 91  
 <212> DNA  
 <213> Homo sapien

<400> 55  
 acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60  
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56  
 <211> 133  
 <212> DNA  
 <213> Homo sapien

<400> 56  
 ggcggatgtg cggttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60  
 tggatttttg gtatctgtgg gttgggggga cggctcagga accaatacc catggatacc 120  
 aagggacaac tgt 133

<210> 57  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 57  
 actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60  
 gactggggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120  
 tctcantggg ctggatncat gcagggt 147

<210> 58  
 <211> 198  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(198)  
 <223> n = A,T,C or G

<400> 58  
 acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60  
 tgattacata catttatcct ttaaaaaaga tgtaaattctt aatttttatg ccattctatta 120  
 atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
 ttgacttcta agtttggt 198

<210> 59  
 <211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59



acaacaaatg	ggttgtgagg	aagtctttatc	agcaaaaactg	gtgatggcta	ctgaaaagat	60
ccattgaaaa	ttatcattaa	tgatttttaa	tgacaagtta	tcaaaaactc	actcaatttt	120
cacctgtgct	agcttgctaa	aatgggagtt	aactctagag	caaatatagt	atcttctgaa	180
tacagtcaat	aaatgacaaa	gccagggcct	acaggtgggt	tccagacttt	ccagacccag	240
cagaaggaat	ctatttttatc	acatggatct	ccgtctgtgc	tcaaaaatacc	taatgatatt	300
tttcgtcttt	attggacttc	tttgaagagt				330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60						
accgtgggtg	ccttctacat	tcttgacggc	tccttcacca	acatctgggt	ctacttcggc	60
gtcgtgggct	ccttcctctt	catectcatc	cagctgggtg	tgctcatcga	ctttgcgcac	120
tcttggaacc	agcggtaggt	gggcaaggcc	gaggagtgcg	attcccgtgc	ctggt	175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61						
acccactttt	tctcctgtg	agcagtctgg	acttctcact	gctacatgat	gagggtgagt	60
ggttgttgct	cttcaacagt	atcctccctt	ttccggatct	gctgagccgg	acagcagtgc	120
tggactgcac	agccccgggg	ctccacattg	ctgt			154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62						
cgctcgagcc	ctatagttag	tcgtattaga				30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63						
acaagtcatt	tcagaccctt	ttgctcttca	aaactgacca	tcttttatat	ttaatgcttc	60
ctgtatgaat	aaaaatgggt	atgtcaagt				89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64						
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aatcagtga	tccaggattg	gtccttggat	ctgggggt			97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
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 gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
 ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggg 180  
 tcggtcataa natgaaatcc caanggggac agaggctcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300  
 tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
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 agaaccctg tgcccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tctctctccc agtcccagc tcaccctcca tccctcacct 180  
 tctctcactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240  
 ttatatattt ttaataaaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120  
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgtgtgtc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tgccctggc	ctggagcccc	aaggaggagg	ataggataat	180
ccggggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctcggggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagtccct	ggggagaaca	480
gaangtcct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccctta	acagggggccc	tctcagccct	cctaatagacc	tccggcctag	ccatgtgatt	60
tcaattccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttcgc	240
agggattttt	ctgagccttt	taccaactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatacagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctatttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaataaagg	tttgtcatct	ttaaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gacctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaa	agtatataag	gctgtaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(511)

<223> n = A,T,C or G

&lt;400&gt; 72

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aaatgaaagg	cttccaggca	gttatctgat	taaagaacac	taaaagagg	acaaggctaa	120
aagccgcagg	atgtctacac	tatancaggc	gctatttggg	ttggctggag	gagctgtgga	180
aaacatggan	agattgggtgc	tgganatcgc	cgtggctatt	cctcattggt	attacanagt	240
gagggttctct	gtgtgcccac	tggtttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaacccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttctaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtgcccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggtg	atgatggcna	480
aaatacaccc	cctcttgaag	naccnggagg	a			511

&lt;210&gt; 73

&lt;211&gt; 499

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (499)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 73

cagtgccagc	actggtgcc	gtaccagtac	caataacagt	gccagtgcc	gtgccagcac	60
cagtgggtggc	ttcagtgtctg	gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	120
tggccttggg	ggagctgggt	ccagcaccag	tggcagctct	gggtgcctgtg	gtttctccta	180
caagtgtgat	tttagatatt	gttaatcctg	ccagtctttc	tcttcaagcc	aggggtgcac	240
ctcagaaacc	tactcaacac	agcactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatctatttg	ccatttctga	aaaaaaaaaa	aaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttaa	acccgctgat	cagcctcgac	tgtgccttct	anttgcagc	420
catctgttgt	ttgccctcc	cccngtgcct	tccttgaccc	tggaaagtgc	cactcccact	480
gtcctttcct	aantaaaat					499

&lt;210&gt; 74

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (537)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggctcaagt	gaatttgaat	actgcattta	cagtgtagag	taacacataa	180
cattgtatgc	atggaaacat	ggaggaacag	tattacagt	tcctaccact	ctaatacaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggcttttgat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgctt	gatataattg	ttgatattaa	gattcttgac	ttatattttg	aatgggttct	420
actgaaaaan	gaatgatata	ttcttgaaga	catcgatata	catttattta	cactcttgat	480
tctacaatgt	agaaaatgaa	ggaaatgccc	caaattgtat	ggtgataaaa	gtcccggt	537

&lt;210&gt; 75

&lt;211&gt; 467

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcattattac acgtacctcc tctgtctcct caagtagtgt ggtctatatt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttctcatcgc gttattgtcc ctagaagcgt cttctgagga 240  
 tctagtgtgg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta 300  
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
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 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120  
 atccagcaga gaatggaaa tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240  
 acttgctctt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 tttagtgagg taaganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
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 ccagctgccc cggcggggga tgcgaggctc ggagcacctc tgcccggctg tgattgctgc 120  
 caggcactgt tcatctcagc ttttctgtcc ctttgtctcc ggcaagcgtc tctgctgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatgget acctttaaca 60  
 tcacccagac cccgccttgc ccgtgcccac cgctgctgct aacgacagta tgatgcttac 120  
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataatgcct 180  
 gatttaaaaa aaaaaaaaaa a 201

<210> 79  
<211> 552  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(552)  
<223> n = A,T,C or G

<400> 79  
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60  
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt 120  
cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatat aaaaaggtag 180  
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240  
atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300  
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360  
taatatctta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta 420  
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac 480  
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540  
aaaaaaaaaa aa 552

<210> 80  
<211> 476  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(476)  
<223> n = A,T,C or G

<400> 80  
acagggtatt gagatgctaa ggccccagag atcgtttgat ccaacctctt tattttcaga 60  
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccttggcct 120  
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180  
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240  
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac 300  
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc 360  
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat 420  
gctgaaaaaa ttaaaatggt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
<211> 232  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(232)  
<223> n = A,T,C or G

<400> 81  
tttttttttg tatgcntcn ctgtgngtt attgttgctg ccaccttga ggagcccagt 60  
ttcttctgta tctttctttt ctgggggagc ttcttggtc tgcccccca ttcccagcct 120  
ctcatcccca tcttgactt ttgctagggg tggaggcgtc ttcttggtag cccctcagag 180  
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct 232

<210> 82  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (383)  
 <223> n = A,T,C or G

<400> 82  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtgc gcagtgccag cactggtgcc 60  
 agtaccagta ccaataacat gccagtgcc gtgccagcac cagtgggtggc ttcagtgtg 120  
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctggtg 180  
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt 240  
 gttaatctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300  
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360  
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (494)  
 <223> n = A,T,C or G

<400> 83  
 accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60  
 gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc 120  
 ccactctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180  
 acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggg ccttaaactg 240  
 atgtcttttc tgccacctgt taccctcgg agactccgta accaaactct tcggactgtg 300  
 agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat 360  
 tatgcttggtg tgaggcaatc atgggtggcat caccatnaa gggaacacat ttganttttt 420  
 tttncatat tttaaattac naccagaata ntccagaata aatgaattga aaaactctta 480  
 aaaaaaaaaa aaaa 494

<210> 84  
 <211> 380  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (380)  
 <223> n = A,T,C or G

<400> 84  
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 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120  
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180  
 gcacaccctc ctggggccca ggccggcacc tgcgtctccc agtatgcaa ctggctggtg 240  
 gtgctgtcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300  
 ccattgtcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360  
 agcgttnccg cctcatccgg 380

<210> 85  
 <211> 481  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(481)  
 <223> n = A,T,C or G

<400> 85  
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctcgc ttcataccgc 60  
 tnccatcgctc atactgtagg ttggccacca cctcctgcat cttggggcgg ctaatatcca 120  
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180  
 tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga 240  
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc 300  
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360  
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420  
 aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnngc gentnccctt 480  
 t 481

<210> 86  
 <211> 472  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(472)  
 <223> n = A,T,C or G

<400> 86  
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60  
 acttggaana gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120  
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180  
 ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240  
 cacaagtcgg aaaaaagcaa aagtaaacag ttnttaattt gtagccaat tcactttctt 300  
 catggggacag agccatttga tttaaaaagc aaattgcata atattgagct ttggggagctg 360  
 atatntgagc ggaagantag cctttctact tcaccagaca caactcctt catattggga 420  
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87  
 <211> 413  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(413)  
 <223> n = A,T,C or G

<400> 87  
 agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatth tgtgtgcgtg 60  
 tgtgtgtgcg cgcataattat atagacaggc acatcttttt tactttttgta aaagcttatg 120  
 cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180  
 ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240  
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300



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ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa 360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt 413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgcttg ccccaactcc cgcgtcccgc 60
gtcctagccn accatggccg ggcccctgcg cgcccctgtg ctctgctgg ccatcctggc 120
cgtggccctg gccgtgagcc ccgcgcccg ctccagtcgc ggcaagccgc cgcgcctggt 180
gggaggccca tggaccccg gtggaagaag aagggtgtgc gcgtgcactg gactttgccg 240
tcggcnanta caacaaacc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc 300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg 420
gaancantcc tgntcttttc caaat ttt 448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca 60
gtagtgattc tgccaaagt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc 120
agaggcttag gtctgcata cagcagacag tttgtccgtg tat tttgtag ccttgaagtt 180
ctcagtgaca agttntttct gatgcgaagt tctnattcca gtgttttagt cctttgcac 240
tttnatgttn agacttgcc ctntnaaatt gcttttgnt tctgcaggta ctatctgtgg 300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn 360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420
aattcnnana anttcagntn tcatacaaca naacngganc ccc 463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctntnt actgtcggac tgttcancca ccaactctac aagttgctgt 60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120
tcttcaccag tcacatcttc taggacctt ttggattcag ttagtataag ctcttccact 180
tcctttgtta agacttcac tggtaaagtc ttaagttttg tagaaaggaa ttttaattgct 240

```

```

cggtctcttaa caatgtcttc tccttgaagt atttggtga acaaccacc tnaagtcct      300
ttgtgcatcc attttaata tacttaatag ggcattggtg cactagggtta aattctgcaa      360
gagtcactctg tctgcaaaag ttgcgttagt atatctgcca                        400

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (480)
<223> n = A,T,C or G

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nmccgctctt      180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaat tcacccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aaccgctgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa      480

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (477)
<223> n = A,T,C or G

<400> 92
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
ggtcccgtct tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt      120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggttggt ggttgacggt      180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgaact gtgcgggacc      240
tgcagcgaaa ctctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg      360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc      420
aggaacggcn ccagcgtgtc caggtcaatg tcgggtgaanc ctccgcgggt aatggcg      477

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (377)
<223> n = A,T,C or G

<400> 93
gaacggctgg accttgctc gcattgtgct gctggcagga ataccttggc aagcagctcc      60
agtccgagca gccccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc      120
cgctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn      180

```

```

tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa      240
caacaacaaa ataacatggt tgctgtttna gttgtataaa agtangtgat tctgtatnta      300
aagaaaatat tactgttaca tatactgctt gcaantttctg tattttattgg tntctctggaa    360
ataaatatat tattaata                                     377

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg gggttagggtc cagttcccag tggaagaaac aggccaggag aantgcgtgc      60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgacccct     120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg     180
gaaggcccca ttccggggct gttcccagag gaggaaggga aggggctctg tgtgcccccc     240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa     300
tgcaagctca ccaaggtccc ctctcagtc ctccctaca ccctgaacgg nacttgccc       360
acacccacc agancancca cccgccatgg ggaatgtnt caaggaatcg cngggcaacg      420
tggaactctng tccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana     480
aaaaaaaaana aaaaaa                                     495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttggt ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt     120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact     180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt     240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta     300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac     360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata     420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at              472

```

```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 96
ctgaagcatt tcttcaaact tntctacttt tgctattgat acctgtagta agttgacaat      60

```

```

gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc ccaagtctt 120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt 180
attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat 240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat 300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
tacaaagtct atcttctca nangtctgtn aaggaacaat ttaatcttct agcttt 476

```

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(479)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

```

actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata 60
aaataatgct gcaaaacttaa tgttcttatg caaaatggaa cgctaatagaa acacagctta 120
caatcgcaaa tcaaaactca caagtgtcct tctgttgtag atttagtgta ataagactta 180
gattgtgctc ctccggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat 240
caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt 300
gtgattatna aattaatcac aaatttctact tatacctgct atcagcagct agaaaaacat 360
ntnnttttta natcaaagta ttttgtgttt ggaantgttn aaatgaaatc tgaatgtggg 420
ttcnatctta ttttttccn gacnactant tnccttttta ggnctattc tganccatc 479

```

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

```

agtgaacttg cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta 60
tgctagtccc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca 120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga 180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatattctca tgcagcttta 240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat 300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaggact 360
ttaagaaaaa ctaccacatg ttgtgtatcc tgggtgccgc cgtttatgaa ctgaccaccc 420
tttggaataa tcttgacgct cctgaacttg ctctctgcg a 461

```

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

```

gtggcgcgc gcaggtgttt cctcgtaccg cagggccccc tcccttcccc aggcgtccct 60
cggcgccctc gcgggcccga ggaggagcgg ctggcgggtg ggggagtggt gaccacccct 120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c 171

```

&lt;210&gt; 100

&lt;211&gt; 269

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 100

cgccgcgaag	tgcaactcca	gctggggccg	tgccgacgaa	gattctgcca	gcagttggtc	60
cgactgcgac	gacggcggcg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggg	gaagcgggag	gcctcgggga	gccctcggg	aagggcggcc	240
cgagagatac	gcaggtgcag	gtggccgcc				269

&lt;210&gt; 101

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttatttttgc	60
gctagcaagg	taacagggt	gggcatggtt	acatgttcag	gtcaacttcc	tttgtcgtgg	120
ttgattgggt	tgtctttatg	ggggcggggg	ggggtagggg	aaacgaagca	aataacatgg	180
agtgggtgca	ccctccctgt	agaacctggt	tacaaagctt	ggggcagttc	acctggtctg	240
tgaccgtcat	tttcttgaca	tcaatgttat	tagaagtcag	gatattcttt	agagagtcca	300
ctgttctgga	gggagattag	ggtttcttgc	caaatccaac	aaaatccact	gaaaaagtgt	360
gatgatcagt	acgaataccg	aggcatattc	tcatatcggt	ggcca		405

&lt;210&gt; 102

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 102

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaattt	aatcccat	tacgggtattt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
atatacttct	ttcagcaaac	ttgttacata	aattaaaaaa	atatatacgg	ctgggtgtttt	240
caaagtacaa	ttatcttaac	actgcaaaca	ttttaaggaa	ctaaaataaa	aaaaaacact	300
ccgcaaaagg	taaagggaac	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttattt	420
ttttaaacca	ttgtttgggc	ccaacacaat	ggaatcccc	ctggactagt		470

&lt;210&gt; 103

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 103

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttatttttact	60
tacacatatt	tatttttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgcttaaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tcttttaaaat	tatctaattc	ttccattttt	tccttatctc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaga	aggcttagat	ccttttatgt	480
ccatttttagt	cactaaacga	tatcaaagtg	ccagaatgca	aaaggtttgt	gaacatttat	540
tcaaaagcta	atataagata	tttcacatac	tcatctttct	g		581

&lt;210&gt; 104

&lt;211&gt; 578

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 104

tttttttttt	tttttttttt	tttttctctt	cttttttttt	gaaatgagga	tcgagttttt	60
cactctctag	atagggcatg	aagaaaactc	atctttccag	ctttaaata	acaatcaa	120
ctcttatgct	atatcatatt	ttaagttaaa	ctaagtgtc	actggcttat	cttctcctga	180
aggaaatctg	ttcattcttc	tcattcatat	agttatatca	agtactacct	tgcatattga	240
gagggtttttc	ttctctattt	acacatatat	ttccatgtga	atttgatca	aacctttatt	300
ttcatgcaaa	ctagaaaata	atgtttcttt	tgcataagag	aagagaacaa	tatagcatta	360
caaaactgct	caaattgttt	gttaagttaa	ccattataat	tagttggcag	gagctaatac	420
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tgaattcaca	tggtattatt	cctagcccaa	cacaatgg			578

&lt;210&gt; 105

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 105

tttttttttt	tttttcagta	ataatcagaa	caatatttat	ttttatat	aaaattcata	60
gaaaagtgcc	ttacatttaa	taaaagtgtg	ttctcctaa	tgatcagagg	aattagatat	120
gtcttgaaca	ccaatattaa	tttgaggaaa	atacaccaaa	atacattaag	taaattattt	180
aagatcatag	agcttgtaag	tgaaaagata	aaatttgacc	tcagaaactc	tgagcattaa	240
aatccacta	ttagcaata	aattactatg	gacttcttgc	tttaattttg	tgatgaatat	300
ggggtgtcac	tggtaaacca	acacattctg	aaggatcat	tacttagtga	tagattctta	360
tgtactttgc	taatacgtgg	atatgagttg	acaagtctct	ctttcttcaa	tcttttaagg	420
ggcgagaaat	gaggaagaaa	agaaaaggat	tacgcatact	gttctttcta	tggaaggatt	480
agatatgttt	cctttgccaa	tattaaaaaa	ataataatgt	ttactactag	tgaaaccc	538

&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 106

tttttttttt	tttttttagtc	aagtttctat	ttttattata	attaaagtct	tggtcatttc	60
atttattagc	tctgcaactt	acatatattaa	attaaagaaa	cgtttttagac	aactgtacaa	120
tttataaatg	taagggtgcca	ttattgagta	atatattcct	ccaagagtgg	atgtgtccct	180
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gcaaacgcta	attctcttct	ccatcccat	gtgatattgt	gtatatgtgt	gagttggtag	300
aatgcatcac	aatctacaat	caacagcaag	atgaagctag	gctgggcttt	cggtgaaaat	360
agactgtgtc	tgtctgaatc	aaatgatctg	acctatcctc	ggtggcaaga	actcttcgaa	420
ccgcttcctc	aaaggcgctg	ccacatttgt	ggctctttgc	acttgtttca	aaa	473

&lt;210&gt; 107

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 107

cgccatggca	ctgcagggca	tctcgggtcat	ggagctgtcc	ggcctggccc	cgggcccgtt	60
ctgtgctatg	gtcctggctg	acttcggggc	gcgtgtggta	cgctgggacc	ggcccggctc	120
ccgctacgac	gtgagccgct	tgggcccggg	caagcgctcg	ctagtgtctg	acctgaagca	180
gccgcgggga	gccgcctgct	tgcggcgtct	gtgcaagcgg	tcggatgtgc	tgctggagcc	240
cttcgcgcgc	ggtgtcatgg	agaaactcca	gctgggcca	gagattctgc	agcgggaaaa	300
tccaaggctt	atttatgcca	ggctgagtgg	atttgccag	tcaggaagct	tctgccggtt	360
agctggccac	gatatcaact	atttgctttt	gtcaggtgtt	ctctcaaaaa	ttggcagaag	420
tggtgagaat	ccgatgccc	cgctgaatct	cctggctgac	tttgctggtg	gtggccttat	480
gtgtgcactg	ggcattataa	tggtcttttt	tgaccgcaca	cgactgaca	agggtcagggt	540

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cattgatgca aatatggtgg aaggaacagc atattttaagt tcttttctgt ggaaaactca 600
gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatggtg gagcaccttt 660
ctatacgact tacaggacag cagatgggga attcatggct gttggagcaa tagaacccca 720
gttctacgag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat 780
gagcatggat gattggccag aaatgaagaa gaagtttgca gatgtatttg caaagaagac 840
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cagccgcgaa gagattttat agcttaactc agataaaatc attgaaagta ataaggtaaa 1140
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aatggttatc attagggctt ttgatttata aaactttggg tacttatact aaattatggt 1380
agttattctg ccttccagtt tgcttgatat atttggtgat attaagattc ttgtattata 1440
ttttgaatgg gttctagtga aaaaggaatg atatattctt gaagacatcg atatacattt 1500
atttacactc ttgattctac aatgtagaaa atgaggaaat gccacaaatt gtatggtgat 1560
aaaagtcacg tgaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
a 1621

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&lt;210&gt; 108

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo. sapien

&lt;400&gt; 108

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Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1      5      10      15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20     25     30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35     40     45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50     55     60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65     70     75     80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145    150    155    160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165    170    175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180    185    190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195    200    205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210    215    220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225    230    235    240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245    250    255

```

Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala  
                   260                  265                  270  
 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp  
                   275                  280                  285  
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val  
                   290                  295                  300  
 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu  
 305                  310                  315                  320  
 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala  
                   325                  330                  335  
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
                   340                  345                  350  
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn  
                   355                  360                  365  
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu  
                   370                  375                  380

&lt;210&gt; 109

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

```

ggcacgaggc tgcgccaggc cctgagcggc ggcgggggca gcctcgccag cggggggcccc      60
gggcctggcc atgcctcact gagccagcgc ctgcgcctct acctcgccga cagctggaac      120
cagtgcgacc tagtggtctt cacctgcttc ctccctggcg tgggctgccc gctgaccccc      180
ggtttgtagc acctggggcg cactgtcttc tgcctcgact tcatggtttt cagggtgccg      240
ctgcttcaca tcttcacggc caacaaacag ctgggggccc agatcgatcat cgtgagcaag      300
atgatgaagg acgtgttctt ctctctcttc ttctctggcg tgtggctggt agcctatggc      360
gtggccacgg aggggctcct gaggccacgg gacagtgact tccaagtat cctgcgccgc      420
gtcttctacc gtccctacct gcagatcttc gggcagattc cccaggagga catggacgtg      480
gccctcatgg agcagagcaa ctgctcgctg gagcccggtc tctgggcaca ccctcctggg      540
gcccgaggcg gcacctgcgt ctcccagtat gccaactggc tgggtggtgct gctcctcgtc      600
atcttctctg tcgtggccaa catcctgctg gtcaacttgc tcattgccat gttcagttac      660
acattcgcca aagtacaggc caacagcgat ctctactgga aggcgcagcg ttaccgcctc      720
atccgggaat tccactctcg gcccgcgctg gcccgcctt ttatcgatcat ctcccacttg      780
cgctcctctg tcaggcaatt gtgcaggcga ccccgagacc cccagccgtc ctcccgggcc      840
ctcgagcatt tccgggttta cctttctaa gaaagccgagc ggaagctgct aacgtgggaa      900
tcgggtgcata aggagaactt tctgctggca cgcgctaggg acaagcgagg gagcgactcc      960
gagcgtctga agcgcacgtc ccagaagggt gacttggcac tgaaacagct gggacacatc     1020
cgcgagtacg aacagcgctt gaaagtgtcg gagcgggagg tccagcagtg tagccgctc     1080
ctgggggtgg tggccgaggc cctgagccgc tctgccttgc tgccccagg tggccgcca     1140
ccccctgacc tgccctgggtc caaagactga gccctgctgg cggacttcaa ggagaagccc     1200
ccacagggga ttttgctcct agagtaaggc tcatctgggc ctcgccccc gcacctggtg     1260
gccttgctct tgaggtgagc cccatgtcca tctgggccac tgtcaggacc acctttggga     1320
gtgtcatcct taaaaccac agcatgccc gctcctccca gaaccagtc cagcctggga     1380
ggatcaaggc ctggatcccc ggccgttatc catctggagg ctgcagggtc cttggggtaa     1440
cagggaccac agaccctca ccactcacag attcctcaca ctggggaaat aaagccattt     1500
cagaggaaaa aaaaaaaaaa aaaa

```

&lt;210&gt; 110

&lt;211&gt; 3410

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 110

```

gggaaccagc ctgcacgcgc tggctccggg tgacagccgc gcgcctcggc caggatctga      60
gtgatgagac gtgtccccac tgaggtgccc cacagcagca ggtgttgagc atgggctgag      120

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aagctggacc	ggcaccaaaag	ggctggcaga	aatggggcgcc	tggctgattc	ctaggcagtt	180
ggcggcagca	aggaggagag	gccgcagctt	ctggagcaga	gccgagacga	agcagttctg	240
gagtgccga	acggccccct	gagccctacc	cgcttgcccc	actatggtcc	agaggctgtg	300
ggtagaccgc	ctgctgcggc	accggaaagc	ccagctcttg	ctggtcaacc	tgctaaccctt	360
tggcctggag	gtgtgttttg	ccgcaggcat	cacctatgtg	ccgcctctgc	tgctggaagt	420
gggggtagag	gagaagttca	tgaccatggt	gctgggcatt	ggtccagtgc	tgggcctggt	480
ctgtgtcccg	ctcctaggct	cagccagtga	ccactggcgt	ggacgctatg	gccgcgcgcg	540
gcccttcac	tgggcactgt	ccttgggcat	cctgctgagc	ctctttctca	tcccaagggc	600
cggtggcta	gcagggtgc	tgtgcccga	tcccaggccc	ctggagctgg	cactgctcat	660
cctgggctg	gggctgctgg	acttctgtgg	ccagggtgtg	ttcactccac	tggaggccct	720
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cggtgccaca	tgctgttccc	acagtgtggc	ctggtgaca	gcttcagccg	ccctcaccgg	1440
gttcaccttc	tcagccctgc	agatcctgcc	ctacacactg	gcctccctct	accaccggga	1500
gaagcaggtg	ttcctgcccc	aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	1560
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cagagacaca	ggcattttaa	tatttaactt	atttatttaa	caaagtagaa	gggaatccat	2640
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gcaggaccag	aagcacaaaag	tgcggttttc	caagcctttg	tccatctcag	ccccagaggt	3120
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gaggtcttat	ctctcagggg	gggtttaagt	gccgtttgca	ataatgtcgt	cttattttatt	3240
tagcgggggtg	aatattttat	actgtaagt	agcaatcaga	gtataatgtt	tatggtgaca	3300
aaattaaagg	ctttcttata	tgtttaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3360
aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaataa	aaaaaaaaaa		3410

&lt;210&gt; 111

&lt;211&gt; 1289

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

```

agccaggcgt ccctctgcct gccactcag tggcaacacc cgggagctgt tttgtccttt      60
gtggagcctc agcagttccc tctttcagaa ctcactgcca agagccctga acaggagcca      120
ccatgcagtg cttcagcttc attaagacca tgatgatcct cttcaatttg ctcactcttc      180
tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcaccccttc      240
tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc      300
tcacgcagc cggcgtttgt gtctttgtct ttggtttcct gggctgctat ggtgctaaga      360
ctgagagcaa gtgtgccctc gtgacgttct tcttcacct cctcctcatc ttcattgctg      420
aggttgagc gcctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt      480
tgctggtagt gctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt      540
ggaacaccac catgaaaggg ctcaagtgtc gtggcttcac caactatacg gattttgagg      600
actcacccta cttcaaagag aacagtgcct tccccccatt ctggtgcaat gacaacgtca      660
ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgacacaaaa gtagagggtt      720
gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag      780
ctggaattgg gggcctcgag ctggctgcca tgattgtgtc catgtatctg tactgcaatc      840
tacaataagt ccacttctgc ctctgccact actgtgcca catgggaact gtgaagagggc      900
accctggcaa gcagcagtga ttgggggagg ggacaggatc taacaatgtc acttggggcca      960
gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg      1020
atgcctgact ttccttccat tgggtgggtgg atgggtgggg ggcattccag agcctctaag      1080
gtagccagtt ctggtgcca tccccccagt ctattaaacc cttgatatgc cccctaggcc      1140
tagtggtgat cccagtgtct tactggggga tgagagaaag gcattttata gcctgggcat      1200
aagtgaaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc      1260
tgttacaatg ttaaaaaaaaa aaaaaaaaaa

```

&lt;210&gt; 112

&lt;211&gt; 315

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

```

Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
 1          5          10          15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
 20          25          30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35          40          45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50          55          60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65          70          75          80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85          90          95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100          105          110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
115          120          125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130          135          140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145          150          155          160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165          170          175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180          185          190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

```

195					200					205					
His	Phe	Arg	Val	Tyr	Leu	Ser	Lys	Glu	Ala	Glu	Arg	Lys	Leu	Leu	Thr
210					215					220					
Trp	Glu	Ser	Val	His	Lys	Glu	Asn	Phe	Leu	Leu	Ala	Arg	Ala	Arg	Asp
225					230					235					240
Lys	Arg	Glu	Ser	Asp	Ser	Glu	Arg	Leu	Lys	Arg	Thr	Ser	Gln	Lys	Val
245					250					255					
Asp	Leu	Ala	Leu	Lys	Gln	Leu	Gly	His	Ile	Arg	Glu	Tyr	Glu	Gln	Arg
260					265					270					
Leu	Lys	Val	Leu	Glu	Arg	Glu	Val	Gln	Gln	Cys	Ser	Arg	Val	Leu	Gly
275					280					285					
Trp	Val	Ala	Glu	Ala	Leu	Ser	Arg	Ser	Ala	Leu	Leu	Pro	Pro	Gly	Gly
290					295					300					
Pro	Pro	Pro	Pro	Asp	Leu	Pro	Gly	Ser	Lys	Asp					
305					310					315					

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<210> 113
<211> 553
<212> PRT
<213> Homo sapien
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	<400>	113													
Met 1	Val	Gln	Arg	Leu 5	Trp	Val	Ser	Arg	Leu 10	Leu	Arg	His	Arg	Lys 15	Ala
Gln	Leu	Leu	Leu 20	Val	Asn	Leu	Leu 25	Thr	Phe	Gly	Leu	Glu	Val 30	Cys	Leu
Ala	Ala	Gly 35	Ile	Thr	Tyr	Val 40	Pro	Pro	Leu	Leu	Leu	Glu 45	Val	Gly	Val
Glu 50	Glu	Lys	Phe	Met	Thr	Met 55	Val	Leu	Gly	Ile	Gly 60	Pro	Val	Leu	Gly
Leu 65	Val	Cys	Val	Pro	Leu	Leu 70	Gly	Ser	Ala	Ser	Asp 75	His	Trp	Arg	Gly
Arg	Tyr	Gly	Arg 85	Arg	Pro	Phe	Ile	Trp 90	Ala	Leu	Ser	Leu 95	Gly	Ile	
Leu	Leu	Ser	Leu 100	Phe	Leu	Ile	Pro 105	Arg	Ala	Gly	Trp	Leu 110	Ala	Gly	Leu
Leu	Cys	Pro 115	Asp	Pro	Arg	Pro 120	Leu	Glu	Leu	Ala	Leu 125	Leu	Ile	Leu	Gly
Val 130	Gly	Leu	Leu	Asp	Phe	Cys 135	Gly	Gln	Val	Cys	Phe 140	Thr	Pro	Leu	Glu
Ala 145	Leu	Leu	Ser	Asp 150	Phe	Arg	Asp	Pro	Asp 155	His	Cys	Arg	Gln	Ala	
Tyr	Ser	Val	Tyr 165	Ala	Phe	Met	Ile	Ser 170	Leu	Gly	Gly 175	Cys	Leu	Gly	Tyr
Leu	Leu	Pro 180	Ala	Ile	Asp	Trp 185	Asp	Thr	Ser	Ala	Leu 190	Ala	Pro	Tyr	Leu
Gly	Thr 195	Gln	Glu	Glu	Cys	Leu 200	Phe	Gly	Leu	Leu	Thr 205	Leu	Ile	Phe	Leu
Thr	Cys 210	Val	Ala	Ala	Thr	Leu 215	Leu	Val	Ala	Glu	Glu 220	Ala	Ala	Leu	Gly
Pro 225	Thr	Glu	Pro	Ala 230	Glu	Gly	Leu	Ser	Ala 235	Pro	Ser	Leu	Ser	Pro	His
Cys	Cys	Pro	Cys 245	Arg	Ala	Arg	Leu	Ala 250	Phe	Arg	Asn 255	Leu	Gly	Ala	Leu
Leu	Pro	Arg 260	Leu	His	Gln	Leu 265	Cys	Cys 265	Arg	Met	Pro 270	Arg	Thr	Leu	Arg
Arg	Leu 275	Phe	Val	Ala	Glu	Leu 280	Cys	Ser	Trp	Met 285	Ala	Leu	Met	Thr	Phe

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130		135		140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp				
145		150		155
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn				
	165		170	175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala				
	180		185	190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile				
	195		200	205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly				
	210		215	220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu				
225		230		235
Gln				240

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
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 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttggtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggg 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360  
 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G

<400> 116  
 acaaagatga accatttctt atattatagc aaaattaaaa tctaccctga ttctaattatt 60  
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcatat tttaagacac atgattttatc ctatttttagt aacctgggtc 180  
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117

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acacatgtcg cttcactgcc ttcttagatg cttctgggtca acatanagga acagggacca      60
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa      120
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaatagcag gatgtgggaa acagatgagg tcacctctgt      240
gactgccccca gcttactgcc thtagagagt ttctangctg cagttcagac agggagaaat      300
tggtt                                             305

```

```

<210> 118
<211> 71
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(71)
<223> n = A,T,C or G

```

```

<400> 118
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa      60
aantcctggg t                                             71

```

```

<210> 119
<211> 212
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(212)
<223> n = A,T,C or G

```

```

<400> 119
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant      180
aatggantca aganactccc aggcctcagc gt                                             212

```

```

<210> 120
<211> 90
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(90)
<223> n = A,T,C or G

```

```

<400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctttgcc      60
ctccgccggc gcagaacatg ctgggggtggt                                             90

```

```

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1) ... (218)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 121

tgtancgtga	anacgacaga	naggggtgtgc	aaaaatggag	aanccttgaa	gtcattttga	60
gaataagatt	tgctaaaaga	tttgggggcta	aaacatgggt	attgggagac	atttctgaag	120
atatncangt	aaattangga	atgaattcat	ggttcttttg	ggaattcett	tacgatngcc	180
agcatanact	tcattgtggg	atancagcta	cccttgta			218

&lt;210&gt; 122

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 122

taggggtgta	tgcaactgta	aggacaaaaa	ttgagactca	actggcttaa	ccaataaagg	60
catttgtag	ctcatggaac	aggaagtcgg	atgggtgggc	atcttcagtg	ctgcatgagt	120
caccaccccg	gcgggggtcat	ctgtgccaca	ggtcctgtt	gacagtgcgg	t	171

&lt;210&gt; 123

&lt;211&gt; 76

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (76)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 123

tgtagcgtga	agacnacaga	atgggtgtgtg	ctgtgctatc	caggaacaca	tttattatca	60
ttatcaanta	ttgtgt					76

&lt;210&gt; 124

&lt;211&gt; 131

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 124

acctttcccc	aaggccaatg	tcctgtgtgc	taactggcgg	gctgcaggac	agctgcaatt	60
caatgtgctg	ggcatatgg	aggggaggag	actctaaaat	agccaatttt	attctcttgg	120
ttaagatttg	t					131

&lt;210&gt; 125

&lt;211&gt; 432

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 125

actttatcta	ctggctatga	aatagatggt	ggaaaattgc	gttaccaact	ataccactgg	60
cttgaaaaag	aggtgatagc	tcttcagagg	acttgtgact	tttgctcaga	tgctgaagaa	120
ctacagtctg	catttggcag	aatgaagat	gaatttggat	taaatgagga	tgctgaagat	180
ttgcctcacc	aaacaaaagt	gaaacaactg	agagaaaatt	ttcaggaaaa	aagacagtgg	240
ctcttgaagt	atcagtcact	tttgagaatg	tttcttagtt	actgcatact	tcattgatcc	300
catggtgggg	gtcttgcac	tgtaagaatg	gaattgattt	tgcttttgca	agaatctcag	360
caggaaacat	cagaaccact	atcttctagc	cctctgtcag	agcaaaccct	agtgcctctc	420
ctctttgctt	gt					432

<210> 126  
<211> 112  
<212> DNA  
<213> Homo sapien

<400> 126  
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
agtaagaatg atatttcccc ccagggatca ccaaataatt ataaaaattt gt 112

<210> 127  
<211> 54  
<212> DNA  
<213> Homo sapien

<400> 127  
accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
<211> 323  
<212> DNA  
<213> Homo sapien

<400> 128  
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60  
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120  
ttctctctga agtctagggt acccattttg gggaccatt ataggcaata aacacagttc 180  
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240  
ttctgcaaaa aggtcactc agtcctttgc ttgtcagtg gactgggctc cccagggcct 300  
aggtgcctt cttttccatg tcc 323

<210> 129  
<211> 192  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(192)  
<223> n = A,T,C or G

<400> 129  
acatacatgt gtgtatatatt ttaaataatca cttttgtatc actctgactt ttagcatac 60  
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120  
tagcacattc atctgtgata naaagatagg tgagtttcat ttcccttcacg ttggccaatg 180  
gataaacaaa gt 192

<210> 130  
<211> 362  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(362)  
<223> n = A,T,C or G

<400> 130  
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60



tataatgacg	caacaaaaag	gtgctgttta	gtcctatggt	tcagtttatg	cccctgacaa	120
gtttccattg	tgttttgccg	atcttctggc	taatcgtggt	atcctccatg	ttattagtaa	180
ttctgtattc	cattttgtta	acgcctggta	gatgtaacct	gctangaggc	taactttata	240
cttattttaa	agctcttatt	ttgtggatcat	taaaatggca	atttatgtgc	agcactttat	300
tgcagcagga	agcacgtgtg	ggttgggtgt	aaagctcttt	gctaacttta	aaaagtaatg	360
gg						362

&lt;210&gt; 131

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttggt	ttaatggagt	ttcccatgca	60
gtangactgg	tatggttgca	gctgtccaga	taaaaacatt	tgaagagctc	caaaatgaga	120
gttctccag	gttcgccctg	ctgtcccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaaat	ctgatgtgat	ttggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactccccan	gacnggtacg	gattgtgggc	300
atanaaggat	tgggtgaagc	tggcgttgtg	gt			332

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

acttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggtctaa	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	agggaagcct	300
gtaacaatct	acaattggtc	ca				322

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

acaagccttc	acaagtttaa	ctaaattggg	attaatcttt	ctgtanttat	ctgcataatt	60
cttggttttc	tttccatctg	gtccttggtg	tgacaatttg	tggaacaaac	tctattgcta	120
ctatttataa	aaaatcacia	atctttccct	ttaagctatg	ttnaattcaa	actattcctg	180
ctattcctgt	tttgtcaaag	aaattatatt	tttcaaaaata	tgtntatttg	tttgatgggt	240

cccacgaaac actaataaaa accacagaga ccagcctg

278

<210> 134  
 <211> 121  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(121)  
 <223> n = A,T,C or G

<400> 134  
 gtttanaaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60  
 tgattctctg aggttaaaact tggttttcaa atgttatatt tacttgtatt ttgcttttgg 120  
 t 121

<210> 135  
 <211> 350  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(350)  
 <223> n = A,T,C or G

<400> 135  
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
 atancaagtg gtgactgggt aagcgtgcga caaagggtcag ctggcacatt acttgtgtgc 120  
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
 ggggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct 240  
 ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgcgtgag 300  
 ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136  
 <211> 399  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(399)  
 <223> n = A,T,C or G

<400> 136  
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt 60  
 gctgtgattg tatccgaata ntctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggtcttga 180  
 cctggcggcc agccagccag ccacaggtgg gcttcttct tttgtggtga caacnccaag 240  
 aaaactgcag agggccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300  
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcagccccac tggcgtgatg 360  
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctggtc ccactggtgg tcactgtcat tggggtgggt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaaggtgc ttgggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120  
 attcaaacag acctcgatc tctggtgtg agcctggctg gctcaccgcc tatcatctgc 180  
 atttgcccta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg 240  
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgccccatcc tccttcacgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaact tgttttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttcatt taacancttt tgttaagtgt caggctgcac tttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 actttatattt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggtttgtt 120  
 atgcatgtag agaaccctaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actantcca atgggggaaa agcaagatgg 300  
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
 gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
 cacatgggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
 ttcaaacatc atagccaatg atgccccgct tgccctataat ctctccgaca taaaaccaca 300  
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcanggggt gggaggaacc agctcaacct tggcggtant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccacca tctcctgag 120  
 accatccgac ttcctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

```

<400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct    60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg    120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt                    164

```

```

<210> 145
<211> 303
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

```

```

<400> 145
acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa    60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat    120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca    180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag    240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat    300
caa                                         303

```

```

<210> 146
<211> 327
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(327)
<223> n = A,T,C or G

```

```

<400> 146
actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gtcctatgac    60
actggcctgg agtgactcat tgcctctggt gggtgagaga gtccttttgc caacaggcct    120
ccaagtcagg gctgggattt gtttccttcc cacattctag caacaatatg ctggccactt    180
cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc    240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg    300
taggggtgag ctgtgtgact ctatggt                                         327

```

```

<210> 147
<211> 173
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(173)
<223> n = A,T,C or G

```

```

<400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg    60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt    120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gtt          173

```

```

<210> 148

```

<211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (477)  
 <223> n = A,T,C or G

<400> 148  
 acaaccactt tatctcatcg aatTTTTaAC ccaaactcac tcaCTgtgcc tttctatcct 60  
 atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120  
 gccctactac ctgctgcaat aatcacattc ccttctgtgc ctgacctga agccattggg 180  
 gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtcac 240  
 nccanccac ctcaccgacc ccacctctct acacagctac ctcttgtctc tctaaccCCA 300  
 tagattatnt ccaaattcag tcaattaagt tactattaac actctaccCG acatgtccag 360  
 caccactggT aagccttctc cagccaacac acacacacac acacncacac acacacatat 420  
 ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg 477

<210> 149  
 <211> 207  
 <212> DNA  
 <213> Homo sapien

<400> 149  
 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60  
 taacgtatnt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct 120  
 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180  
 tttcaggcag agggaacagc agtgaaa 207

<210> 150  
 <211> 111  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (111)  
 <223> n = A,T,C or G

<400> 150  
 accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60  
 cacttaaatt tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151  
 <211> 196  
 <212> DNA  
 <213> Homo sapien

<400> 151  
 agcgcggcag gtcatttga acattccaga tacctatcat tactcgatgc tgttgataac 60  
 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaacCAT 120  
 ggataccaac cggaaaaccC ctatcccgca cagccactg tggTccccac tgtctacgag 180  
 gtgcateccg ctcagt 196

<210> 152  
 <211> 132  
 <212> DNA

<213> Homo sapien

<400> 152

acagcacttt	cacatgtaag	aagggagaaa	ttcctaaatg	taggagaaag	ataacagAAC	60
cttccccctt	tcatctagt	gtggaaacct	gatgctttat	gttgacagga	atagaaccag	120
gagggagttt	gt					132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (285)

<223> n = A,T,C or G

<400> 153

acaanacca	nganaggcca	ctggccgtgg	tgctcatggc	tccaaacatg	aaagtgtcag	60
cttctgctct	tatgtcctca	tctgacaact	ctttaccatt	tttatcctcg	ctcagcagga	120
gcacatcaat	aaagtccaaa	gtcttggaact	tggccttggc	ttggaggaag	tcatcaaac	180
cctggctagt	gaggggtgcg	cgccgctcct	ggatgacggc	atctgtgaag	tcgtgcacca	240
gtctgcaggc	cctgtggaag	cgccgtccac	acggagtnag	gaatt		285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc	tggtgggcca	gggcttcatg	accctttctg	tgaaaagcca	tattatcacc	60
accccaaat	tttccttaa	tatctttaac	tgaaggggtc	agcctcttga	ctgcaaagac	120
cctaagccgg	ttacacagct	aactcccact	ggccctgatt	tggtgaaattg	ctgctgcctg	180
attggcacag	gagtcgaagg	tggttcagtc	ccctcctccg	tggaacgaga	ctctgatttg	240
agtttcacaa	attctcgggc	cacctcgta	ttgctcctct	gaaataaaat	ccggagaatg	300
gtcaggcctg	tctcatccat	atggatcttc	cgg			333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (308)

<223> n = A,T,C or G

<400> 155

actggaaata	ataaaaccca	catcacagt	ttgtgtcaaa	gatcatcagg	gcatggatgg	60
gaaagtgcct	tggggaactg	aaagtgccta	acacatgatc	gatgattttt	gttataatat	120
ttgaatcacg	gtgcatacaa	actctcctgc	ctgctcctcc	tgggccccag	ccccagcccc	180
atcacagctc	actgctctgt	tcatccaggc	ccagcatgta	gtggctgatt	cttcttggct	240
gcttttagcc	tccanaagtt	tctctgaagc	caaccaaacc	tctangtgta	aggcatgctg	300
gccctgggt						308

<210> 156

<211> 295

<212> DNA

<213> Homo sapien

<400> 156

accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta	60
ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaactga	120
gaataggaga ttatgtttgg cctcatatt ctctcctatc ctcttgcct cattctatgt	180
ctaataatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat	240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat	295

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

acaagtttaa atagtgtgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct	60
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc	120
cttagt	126

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(442)

<223> n = A,T,C or G

<400> 158

accactgggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg	60
aanccagcag gctgcccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt	120
gctggggtaa ttcaccatta atttctctcc ccaaactctc tgagtcttcc cttaatatatt	180
ctgggtggttc tgaccaaagc aggtcatggt ttgttgagca ttggggatcc cagtgaagta	240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg	300
ccaaccctgt ttccccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga	360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg	420
tgttcattct ctgatgtcct gt	442

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc	60
tccaacaaga actgaggttg cagagcgggt agggaaagat gctgttccag ttgcacctgg	120
gctgctgtgg actgttgttg attcctcact acggccaag gttgtggaac tggcanaaag	180
gtgtgttgtt gganttgagc tcgggcggct gtggtagggt gtgggctctt caacaggggc	240
tgctgtgggt cggggangtg aangtgttgt gtcacttgag cttggccagc tctggaaagt	300
antanattct tcctgaaggc cagcgttgtt ggagctggca ngggtcantg ttgtgtgtaa	360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn	420
tcaggttaana atgtggtttc agtgtccctg ggngctgtg gaaggttgta nattgtcacc	480



aagggaataa gctgtggt 498

<210> 160  
 <211> 380  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(380)  
 <223> n = A,T,C or G

<400> 160  
 acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac 60  
 agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct 120  
 ggagcatggc atagaggaag ctganaaatg tgggggtctga ggaagccatt tgagtctggc 180  
 cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc 240  
 ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300  
 gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa 360  
 cttgtagaat gaagcctgga 380

<210> 161  
 <211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 161  
 actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca 60  
 cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt 114

<210> 162  
 <211> 177  
 <212> DNA  
 <213> Homo sapien

<400> 162  
 actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa 60  
 gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120  
 tgggtgatata taacttggca ataaccagct ctggtgatac ataaaactac tcaactgt 177

<210> 163  
 <211> 137  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(137)  
 <223> n = A,T,C or G

<400> 163  
 catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60  
 canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120  
 catcagcggc atgatgt 137

<210> 164  
 <211> 469  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacia	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacett	cgtgacttta	60
tgcaatgcat	catgctat	catacctaat	gagggagttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacaccca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	caaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgt	360
tctagtaggc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacacttt		469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgccgg	cacttgtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggctag	agtaaaaatt	attcttatag	cccatgtccc	120
tgcaggccgc	ccgccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcgga	gtccacacca	ccggtgtagg	tgtgctcaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgagacc	agcctgagca	aggggcggat	gttcagcttc	agtcctcct	tcgtcaggtg	240
gatgccaacc	tcgtctangg	tccgtgggaa	gctgggtgtcc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc 180  
 aattcccaac ttccttgcca caagcttccc aggcctttctc ccctggaaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgccttgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgaccccc atacttctc aaaggctgtg gtaagttttg cacaggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

&lt;400&gt; 170

```

acctgtgggc tgggctgtta tgcctgtgcc ggctgtgtgaa agggagtcca gaggtggagc      60
tcaaggagct ctgcaggcat ttgtccaanc ctctccanag canagggagc aacctacact      120
ccccgctaga aagacaccag attggagctc tgggaggggg agttgggggtg ggcatttgat      180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct      240
tcaaagctag gggctctggca ggtgga                                     266

```

&lt;210&gt; 171

&lt;211&gt; 1248

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1248)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 171

```

ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca      60
ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcacccgca gtgggtgctg      120
tcagccgcac actgtttcca gaagtgaagt cagagctcct acaccatcgg gctgggcctg      180
cacagtcttg aggcgacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc      360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtcggtgggt tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc ggcgaggagg aagaccagaa ggactcctgc      540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc      600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc      660
actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccccctct      780
ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc      840
cccagcccct cctccctcag acccaggagt ccagacccc cagccccctc tccctcagac      900
ccaggagtcc agccccctct ccctcagacc caggagtcca gacccccag cccctcctcc      960
ctcagaccca ggggtccagg cccccaaccc ctctcctc agactcagag gtccaagccc      1020
ccaaccntc attccccaga ccagagggtc cagggtccag cccctcntcc ctcagaccca      1080
gcggtccaat gccacctaga cnttccctgt acacagtgcc cccttggtggc acgttgaccc      1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1248

```

&lt;210&gt; 172

&lt;211&gt; 159

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(159)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 172

```

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1              5              10              15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
      20              25              30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
      35              40              45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

```

50					55					60					
Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu
65					70					75					80
Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe
				85					90					95	
Cys	Ala	Gly	Gly	Gln	Xaa	Gln	Xaa	Asp	Ser	Cys	Asn	Gly	Asp	Ser	
			100				105					110			
Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe
		115				120					125				
Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn
	130				135					140					
Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser	
145				150					155						

&lt;210&gt; 173

&lt;211&gt; 1265

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1265)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 173

ggcagcccg	actgcagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgttctgc	60
tggggcgctcc	tgggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc	120
tacaccatcg	ggctgggcct	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gacccttgct	cgctaacgac	240
ctcatgtctca	tcaagttgga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgccctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggaggtcctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgcgtcccag	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggg	ggtgtctgag	gaggtctgca	gtaagctcta	tgaccgcgtg	taccacccca	540
gcattgtctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggg	gactctgggg	600
ggccccgat	ctgcaacggg	tacttgacgg	gccttggtgc	tttcggaaaa	gccccgtgtg	660
gccaaagtgg	cgtgcacagg	gtctacacca	acctctgcaa	attcactgag	tggatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaaattgac	ccccaaatac	780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tctcctccta	ggcccaggag	840
tccaggcccc	cagccctcc	tccctcaaac	caagggatca	gatccccagc	ccctcctccc	900
tcagaccag	gagtccagac	ccccagcccc	ctcctcctc	agaccagga	gtccagcccc	960
tctcctntca	gaccagagg	tccagacccc	ccagccctc	ctcctcaga	cccaggggtt	1020
gaggccccca	acccctcctc	cttcagagtc	agagggtccaa	gcccccaacc	cctcgttccc	1080
cagaccagga	ggttnnaggtc	ccagccctc	tccctcaga	cccagnggtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggngngttg	acccaacctt	accagttggt	1200
ttttcatttt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

&lt;210&gt; 174

&lt;211&gt; 1459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1459)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 174

```

ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggccc 60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120
tacggcaccac agagtacaac agacccttgc tcgctaacga cctcatgctc atcaagttgg 180
acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcctta 240
ccgcgggggaa ctcttgctc gtttctggct ggggtctgct ggcgaacggg gagctcacgg 300
gtgtgtgtct gccctcttca aggaggctct ctgcccagtc gcgggggctg acccagagct 360
ctgctgcccc ggagaaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420
ngagggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg 480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540
caggggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600
atggagagac acacagggag acagtgacaa cttagagagag aaactgagag aaacagagaa 660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggg 780
gacctccacc caatagaaaa tctctttata acttttgact ccccaaaaac ctgactagaa 840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900
tttatgcatt catgatatac ctttgttggg attttttgat atttctaagc tacacagttc 960
gtctgtgaat ttttttaaata tgttgcaact ctctaaaat ttttctgatg tgtttattga 1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080
gtaccacagag ggaaacagtg acacagattc atagagtgta aacacgaaga gaaacaggaa 1140
aatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaac ccagcacttt 1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380
gaagtgaatt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440
caaaaaaaaa aaaaaaaaaa

```

&lt;210&gt; 175

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (1167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 175

```

ggcgagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgctcctg 60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc 240
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 300
tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360
atgcctaccg tgctgcactg cgtgaacgtg tcggtgggtg ctgaggangt ctgcagtaag 420
ctctatgacc cgtgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 480
gactcctgca acggtgactc tggggggccc ctgactcgca acgggtactt gcagggcctt 540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc cagggtgtcta caccaacctc 600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gtttaactctg gggactggga 660
acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720
gcccctctc cctcaggccc aggagtccag gccccagcc cctcctccct caaaccaagg 780
gtacagatcc ccagcccctc ctccctcaga ccaggagtc cagaccccc agccccctnt 840
ccntcagacc caggagtcca gcccctcctc cntcagacg aggagtccag accccccagc 900
ccntctcgg tcagaccagc ggggtgcagg ccccaacccc tcntcntca ggtcagagg 960
tccaagcccc caaccctcg tccccagac ccagaggtnc aggtcccagc cctcctccc 1020
tcagaccagc cgttccaatg ccacctagan tntcctgta cacagtgecc ccttgtggca 1080
ngttgaccca accttaccag ttggttttct attttttgct cctttccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa

```

1167

<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

<400> 176  
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  
 1 5 10 15  
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
 20 25 30  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val  
 35 40 45  
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu  
 50 55 60  
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
 65 70 75 80  
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly  
 85 90 95  
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met  
 100 105 110  
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val  
 115 120 125  
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala  
 130 135 140  
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly  
 145 150 155 160  
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys  
 165 170 175  
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys  
 180 185 190  
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser  
 195 200 205

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

<400> 177  
 gcgcactcgc agccctggca ggccggcactg gtcattggaaa acgaattggt ctgctcgggc 60  
 gtcttggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctctacacc 120  
 atcgggctgg gctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag 180  
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240  
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300  
 tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctggggtct gctggcgaac 360  
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420  
 caaccctggc aggggtgtac catttcggca acttccagtg caaggacgtc ctgctgcatc 480  
 ctactggtg gctcactact gctcactgca tcaccgcgaa cactgtgata aactagccag 540  
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600  
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660  
 cagttatcct cactgaattg agatttcctg cttcagtgct agccattccc acataatttc 720  
 tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa 780

```

ttcattttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttta atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa     1119

```

<210> 178  
 <211> 164  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1) ... (164)  
 <223> Xaa = Any Amino Acid

```

<400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1              5              10              15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
      20              25              30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
      35              40              45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
      50              55              60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
      65              70              75              80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
      85              90              95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
      100             105             110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
      115             120             125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
      130             135             140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
      145             150             155             160
Pro Gly Thr Leu

```

<210> 179  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

```

<400> 179
ctggagtgcc ttggtgtttc aagcccttgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct     120
gccaggcact gtcatctca gcttttctgt ccctttgtct ccggcaagcg cttctgctga     180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa     240
aaaaaaaaaa                                     250

```

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien



```

<400> 180
actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatgggt acctttaaca    60
tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta    120
ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc    180
tgatttaaaa aaaaaaaaaa aa                                           202

```

<210> 181

<211> 558

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (558)

<223> n = A,T,C or G

```

<400> 181
tccytttktg naggtttkkg agacamceck agacctwaan ctgtgtcaca gacttcyngg    60
aatgttttag cagtgtctagt aatttctytcg taatgattct gttattactt tcctnattct    120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa    180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca    240
aaattatgca agttagtaat tactcagggg taactaaatt actttaatat gctgttgaac    300
ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa    360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw    420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt    480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc    540
caaaaaaaaa aaaaaaaaaa                                           558

```

<210> 182

<211> 479

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (479)

<223> n = A,T,C or G

```

<400> 182
acagggwttk grggatgcta agscccerga rwtggtttga tccaaccctg gcttwttttc    60
agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg    120
cstcacacag astcccaggt agctgggact acaggcacac agtcactgaa gcaggccctg    180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca    240
ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca    300
tactmttcta agtcctcttc cagcctcact kkgagtcctm cytggggggt gataggaant    360
ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara    420
awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa    479

```

<210> 183

<211> 384

<212> DNA

<213> Homo sapien

<400> 183

```

aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc    60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgtc    120
ggtgccagcc tgaccgccac tctcacattt yggctcttcg ctggccttgg tggagctggg    180
gccagcacca gtggcagctc tgggtgctgt gggttctctc acaagtgaga ttttagatat    240

```

```

tggttaatcct gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca   300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt   360
gccatttcaa aaaaaaaaaa aaaa                                           384

```

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (496)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 184

```

accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc   60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag   120
cccattctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga   180
aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac   240
tgatgtcttt tctgccacct gttaccctc ggagactccg taaccaaact cttcggactg   300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg   360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt   420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst   480
taaaaaaaaa aaaaaa                                           496

```

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 185

```

gctggtagcc tatggcgkgg ccacaggagg ggctcctgag gccacggrac agtgacttcc   60
caagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc   120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct   180
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg   240
tgggtgctgt cctcgtcatc ttctgctcgt tggccaacat cctgctggtc aacttgctca   300
ttgccatggt cagttacaca ttcgggcaaag tacagggcaa cagcgatctc tactgggaag   360
cgcgagcgtt accgcctcat ccgg                                           384

```

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

```

gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggccctctcg ttcataccgc   60
tnccatcgtc atactgtagg ttggccacca cytcttgcca tcttggggcg gcntaatatt   120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttccgc   180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgaactt   240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgagggtcac   300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttggtgtg gggkkgaagt   360
ctcaccaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgcccag   420
gtggaaaaaag amcamctcct ggargtgctn gccgctctc gtcmgttggt ggcagcgctw   480

```

```

tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540
aagatntcgc acagcactna tccagttggg attaaat 577

```

```

<210> 187
<211> 534
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(534)
<223> n = A,T,C or G

```

```

<400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw 60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggtg 180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt 240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag ctttggggagc 360
tgatatttga gcggaagagt agccttttcta cttcaccaga cacaactccc tttcatattg 420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttcgtttctg 480
aggatctccc agtttattta ccacttgcac aagaaggcgt tttcttcctc aggc 534

```

```

<210> 188
<211> 761
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(761)
<223> n = A,T,C or G

```

```

<400> 188
agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatth ttgtgtgcgtg 60
tgtgtgtgctg cgcataattat atagacaggc acatcttttt tactttttgta aaagcttatg 120
cctcttttggc atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
ttgtcttctg tgtaaagtgt actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa ttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctgggtgaga arttgcataa 360
acagaaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtkttt wttctccctt 420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480
cttgcccttc attacatggt tnaaagtggg gtgggtgggcc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaatata ctttgaacta 660
ttttctgtn ttccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaaataata acattgaaga aaananaaaa aaanaaaaaa a 761

```

```

<210> 189
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

```

&lt;400&gt; 189

tttttttttt	tttgccgatn	ctactat	tttt	attgcaggan	gtgggggtgt	atgcaccgca	60
caccgggget	atnagaagca	agaaggaagg	agggagggca	cagccccttg	ctgagcaaca		120
aagccgctg	ctgccttetc	tgtctgtetc	ctggtgcagg	cacatgggga	gaccttcccc		180
aaggcagggg	ccaccagtcc	aggggtggga	atacaggggg	tgggangtgt	gcataagaag		240
tgataggcac	aggccacccg	gtacagaccc	ctcggctcct	gacaggtnga	tttcgaccag		300
gtcattgtgc	cctgcccagg	cacagcgtn	atctggaaaa	gacagaatgc	tttccttttc		360
aaatttggt	ngtcatngaa	ngggcanttt	tccaanttng	gctnggtctt	ggtacncttg		420
gttcggccca	gtccncgtc	caaaaantat	tcaccennct	ccnaattgct	tgcnngnccc		480
cc							482

&lt;210&gt; 190

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (471)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 190

tttttttttt	ttttaaaaca	gtttttcaca	acaaaattta	ttagaagaat	agtggttttg	60
aaaactctcg	catccagtga	gaactaccat	acaccacatt	acagctngga	atgtntctcca	120
aatgtctggt	caaattgatac	aattggaacca	ttcaatctta	cacatgcacg	aaagaacaag	180
cgcttttgac	atacaatgca	caaaaaaaaa	aggggggggg	gaccacatgg	attaaaattt	240
taagtactca	tcacatacat	taagacacag	ttctagtcca	gtcnaaaatc	agaactgcnt	300
tgaaaaattt	catgtatgca	atccaaccaa	agaacttnat	tggtgatcat	gantnctcta	360
ctacatcnac	cttgcatt	gccaggaacn	aaaagttnaa	ancacnngt	acaaaaanaa	420
tctgtaattn	anttcaacct	ccgtacngaa	aatnttnt	tatacactcc	c	471

&lt;210&gt; 191

&lt;211&gt; 402

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (402)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 191

gagggattga	aggtctgttc	tastgtcggm	ctgttcagcc	accaactcta	acaagttgct	60
gtcttcact	cactgtctgt	aagcttttta	accagacwg	tatcttcata	aatagaacaa	120
attcttcacc	agtcacatct	tctaggacct	ttttggattc	agttagtata	agctcttcca	180
cttcctttgt	taagacttca	tctggtaaag	tcttaagt	tgtagaaagg	aattyaattg	240
ctcgttctct	aacaatgtcc	tctccttgaa	gtatttggct	gaacaacca	cctaaagtcc	300
ctttgtgcat	ccatttttaa	tatacttaat	agggcattgk	tncactaggt	taaattctgc	360
aagagtcac	tgtctgcaaa	agttgcgtta	gtatatctgc	ca		402

&lt;210&gt; 192

&lt;211&gt; 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 192

```

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatcccggt      180
cttttgaggga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc      240
acgagacact tgaaagggtg aacaaagcga ytcttgcatg gctttttgtc cctccggcac      300
cagttgtcaa tactaacccg ctgggttgcc tccatcacat ttgtgatctg tagctctgga      360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarg tcttggtgcc      420
tggtggatca gggtcccatg tcccagtcyg aatgttcaca tggcatatgt wacttcccac      480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag      540
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag ccccaccagc agcagaagca      600
g

```

&lt;210&gt; 193

&lt;211&gt; 608

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (608)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 193

```

atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt      120
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg      180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac      240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc      300
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcggcctcg      360
gaccagcgga caaacggcrt tgaacagccg cacctcacgg atgcccagtg tgtcgcgctc      420
caggammgsc accagcgtgt ccagggtcaat gtccgtgaag ccctccgcgg gtrattggcg      480
ctgcagtggt tttgtcgatg ttctccaggg acaggctggc cagctgcggg tcacggaaga      540
gtcgcgctcg cgtgagcagc atgaaggcgt tgtcggtcgc cagttcttct tcaggaacte      600
cacgcaat

```

&lt;210&gt; 194

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (392)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 194

```

gaacggctgg accttgcttc gcatttgtct tgcgtggcagg gaataccttg gcaagcagyt      60
ccagtcggag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggcttcccc      120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg      180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac      240
aacaacaaca aaataacatg tttgcctggt aagttgtata aaagtaggtg attctgtatt      300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktinctstgg      360
aaataaatat agttattaaa ggttgctcant cc

```

<210> 195  
 <211> 502  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(502)  
 <223> n = A,T,C or G

<400> 195  
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60  
 ccgagctgag gcagatgttc ccacagtgc cccagagcc stgggstata gtytctgacc 120  
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180  
 aaggggaaggc cccattccgg ggstgttccc cgaggaggaa ggggaaggggc tctgtgtgcc 240  
 ccccasgagg aagaggccct gagtccctggg atcagacacc ccttcacgtg tatccccaca 300  
 caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact 360  
 gscscacacc caccagagc acgccaccgc ccatggggar tgtgtctcaag gartcgcnng 420  
 gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480  
 gctnanaaaa aaaaaaaaaa aa 502

<210> 196  
 <211> 665  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(665)  
 <223> n = A,T,C or G

<400> 196  
 ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60  
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120  
 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180  
 actwatthtat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac 240  
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300  
 attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttctaact 360  
 tcaacttggt attttattgt aatgattta caaaattctt aatttaagar aatggatgt 420  
 watatttatt tcattaattt ctttcctkgt ttacgtwaat ttgaaaaga wtgcatgatt 480  
 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540  
 ttcttagaat gtataaagg ttagcccat cnaacttcaa agaaaaaat gaccacatac 600  
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660  
 aagtg 665

<210> 197  
 <211> 492  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(492)  
 <223> n = A,T,C or G

<400> 197  
 ttttnttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat 60  
 atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtna gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccttgaaact tactccatcc aaatatggga ataanagtca gcagtgtac      300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg      480
ancntggctt aa

```

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (478)

<223> n = A,T,C or G

<400> 198

```

tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagttttaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatgggtta gaatcgtaca cttatgttta catatgtnc      420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa      478

```

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (482)

<223> n = A,T,C or G

<400> 199

```

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcaactgaca atcagaccta      60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttctcttac ggatgagaga ctggctcaag aatatactca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggctttngg ctggggacca tccattgaa ccttctctta      360
anggacttta agaanaaact accacatgtn tgtngtatcc tgggtgccngg ccgtttantg      420
aacntngacn ncacccttnt ggaatanant cttgacngcn tectgaactt gctcctctgc      480
ga

```

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (270)

<223> n = A,T,C or G

```

<400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc      60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc      120
aaggctgagc tgacgccgca gaggtcgtgt cactgccac gaccttgacg ccgtcgggga      180
cagccggaac agagcccggt gaangcggga ggcctcgggg agccctcgg gaagggcggc      240
ccgagagata cgcaggtgca ggtggccgcc
                                                                270

```

```

<210> 201
<211> 419
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(419)
<223> n = A,T,C or G

```

```

<400> 201
tttttttttt ttttgaatc tactgcgagc acagcaggtc agcaacaagt ttatttttgc      60
gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg      120
ttgattggtt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca      180
tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg      240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag      300
tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaa atccacntga      360
aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cggtgggcca      419

```

```

<210> 202
<211> 509
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(509)
<223> n = A,T,C or G

```

```

<400> 202
tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng      120
gtntttttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa      180
tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa      240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atnttttnaa      300
ggaactaaaa taaaaaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta      360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng      420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca      480
caatggnaat nccnccnncn tggactagt
                                                                509

```

```

<210> 203
<211> 583
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(583)
<223> n = A,T,C or G

```



```

<400> 203
tttttttttt ttttttttga ccccccctctt ataaaaaaca agttaccatt ttatttttact    60
tacacatatt tattttataa ttgggtattag atattcaaaa ggcagctttt aaaatcaaac    120
taaattgaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt    180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc    240
atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt    300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa    360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc    420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg    480
tccatttttag tcaactaaac atatcnaaag tgccagaatg caaaagggtt gtgaacattt    540
attcaaaagc taatataaga tatttcacat actcatcttt ctg                          583

```

<210> 204

<211> 589

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (589)

<223> n = A,T,C or G

```

<400> 204
ttttttttnt tttttttttt ttttttnctc ttcttttttt ttganaatga ggatcgagtt    60
tttcactctc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca    120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc    180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat    240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccctt    300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag    360
cattacaaaa ctgctcaaat tgtttgtaa gnttatccat tataattagt tnggcaggag    420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc    480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat    540
ttattnagaa tgaattcaca tgttattatt cnttagccca acacaatgg                          589

```

<210> 205

<211> 545

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (545)

<223> n = A,T,C or G

```

<400> 205
ttttnttttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat    60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata    120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat    180
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt    240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat    300
atgggggtgc actggtaaac caacacattc tgaaggatac attacttagt gatagattct    360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt    420
aaggggngca ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg    480
aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga    540
aacc                                              545

```

<210> 206

<211> 487

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(487)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 206

tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt	60
cattttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna	120
caatttataa atgtaagggtg ccattattga gtanatatat tcctccaaga gtggatgtgt	180
cccttctccc accaactaat gaancagcaa cattagtta attttattag tagatnatac	240
actgtgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag	300
ttggtnagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt	360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag	420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt	480
ttcaaaa	487

&lt;210&gt; 207

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 207

tgaattgggt aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa	60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact	120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana	180
atctttgcat gcagaggagg taaaagggtat tggattttca cagaggaana acacagcgca	240
gaaatgaagg ggcagggtt actgagcttg tccactggag ggctcatggg tgggacatgg	300
aaaagaaggc agcctaggcc ctggggagcc ca	332

&lt;210&gt; 208

&lt;211&gt; 524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(524)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 208

agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg	60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat	120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac	180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaataact	240
tttggcagaa tacttnttga aacttcgaga tgataactaa gatccaagat atttcccaaa	300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgatcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209  
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcatte ttgctccttg 60  
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120  
 caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (256)  
 <223> n = A,T,C or G

<400> 210  
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60  
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120  
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180  
 ttgcaggggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240  
 ccaggatgct aaatca 256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (264)  
 <223> n = A,T,C or G

<400> 211  
 acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga 180  
 ggggagatac attcngaaa aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240  
 aaaaaaggag caaatgagaa gcct 264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgcag 180

ttnaatttca ttccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta	240
cccctacnac tctttactct ctggnaggg ccagtgggtg tagctataag cttggccaca	300
tttttttttc ctttattcct ttgtcaga	328

&lt;210&gt; 213

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 213

acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt	60
taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct	120
cattatgcc aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt	180
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct	240
tctcatcggt	250

&lt;210&gt; 214

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 214

accagaate caatgctgaa tatttggtt cattattccc agattctttg attgtcaaag	60
gatttaattg tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg	120
tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt	180
tgaatttcat tccattgac ttgggatcct tatcatcage canagagatt gaaaatttac	240
ccctacgact ctttactctc tggagagggc cagtgggtgt agctataagc ttggccacat	300
ttttttttcc tttattcctt tgctcagagat gcgattcctc catatgctan aaaccaacag	360
agtgaactttt acaaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt	420
actttgctct ccctaataata cctc	444

&lt;210&gt; 215

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(366)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 215

acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt	60
taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct	120
cattatgcc aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt	180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatata tctctgacct	240
tctcatcggt aagcagaggc ttaggcaac atggaccata gcgaanaaaa aacttagtaa	300
tccaagctgt tttctacact gtaaccagggt ttccaaccaa ggtggaaatc tctatactt	360

ggtgcc

366

&lt;210&gt; 216

&lt;211&gt; 260

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(260)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 216

ctgtataaac	agaactccac	tgcanagagg	agggccgggc	caggagaatc	tccgcttgtc	60
caagacaggg	gcctaaggag	ggtctccaca	ctgctnntaa	gggctnttnc	atttttttat	120
taataaaaag	tnnaaaaggc	ctcttctcaa	cttttttccc	ttnggctgga	aaatttaaaa	180
atcaaaaatt	tctnaagtt	ntcaagctat	catatatact	ntatcctgaa	aaagcaacat	240
aattcttctt	tccctccttt					260

&lt;210&gt; 217

&lt;211&gt; 262

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(262)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 217

acctacgtgg	gtaagtttan	aaatgttata	atttcaggaa	naggaacgca	tataattgta	60
tcttgcttat	aattttctat	tttaataagg	aaatagcaaa	ttgggggtggg	gggaatgtag	120
ggcattctac	agtttgagca	aaatgcaatt	aaatgtggaa	ggacagcact	gaaaaatttt	180
atgaataatc	tgtatgatta	tatgtctcta	gagtagattt	ataattagcc	acttacccta	240
atatacttca	tgcttgtaaa	gt				262

&lt;210&gt; 218

&lt;211&gt; 205

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(205)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 218

accaaggtgg	tgctattaccg	gaantggatc	aangacacca	tcgtggccaa	cccctgagca	60
cccctatcaa	ctcccctttg	tagtaaaactt	ggaaccttgg	aaatgaccag	gccaaagactc	120
aggcctcccc	agttctactg	acctttgtcc	ttangtntna	ngtccagggt	tgctaggaaa	180
anaaatcagc	agacacaggt	gtaaa				205

&lt;210&gt; 219

&lt;211&gt; 114

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 219

tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg gccccatcca 60  
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
<211> 93  
<212> DNA  
<213> Homo sapien

<400> 220  
actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60  
aaataagcat ttagtgctca gtccctactg agt 93

<210> 221  
<211> 167  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (167)  
<223> n = A,T,C or G

<400> 221  
actangtgca ggtgcgcaca aatatttgct gatattccct tcattcttga ttccatgagg 60  
tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120  
ccccactac cttccctgac gctcccccana aatcacccaa cctctgt 167

<210> 222  
<211> 351  
<212> DNA  
<213> Homo sapien

<400> 222  
agggcgtggt gcggaggggc gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
gttcttcacc tgtccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120  
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
taggtgagca tgattagaga gcttgtaggt tgcctttaca tatatctggc atatttgagt 300  
ctcgatatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
<211> 383  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (383)  
<223> n = A,T,C or G

<400> 223  
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
tggtaattat ggtcaattta atwrttrtkk ggggcatttc cttacattgt cttgacaaga 120  
ttaaagtgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc 180  
tgccaaagga agtctaagga attagtagtg ttcccmteac ttgtttggag tgtgctatgc 240  
taaaagattt tgatttcctg gaatgacaat tatattttta ctttgggtggg ggaaanagtt 300  
ataggaccac agtcttcact tctgatactt gtaaattaat cttttattgc acttgttttg 360  
accattaagc tatatgttta aaa 383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

<400> 224  
 cccctgaagg cttcttggtta gaaaatagta cagttacaac caataggaac aacaaaaaga 60  
 aaaagtttgt gacattgttag tagggagtggt gtacccctta ctcccatca aaaaaaaaaat 120  
 ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180  
 gagaaaatac tactttctcr aaatggaagc ccttaaagggt gctttgatac tgaaggacac 240  
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 tttaractcm gcattgtgac 320

<210> 225  
 <211> 1214  
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 <213> Homo sapien

<400> 225  
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 aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180  
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 aaaaaaaaaa aaaa 1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

<400> 226  
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 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<400> 227  
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gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
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aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

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gtcatgacgt	ttgacatacc	tttggaacga	gcctcctcct	tgggaagatgg	aagaccgtgt	120
tctgtggcga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
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tgtcgggtgc	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
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gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
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&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

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cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcaggggtg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagctc	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcctgggtca	cactcaggaa	cgagagctga	cccagtttaag	ggagaagttg	180
cggaagggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301



<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

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 caggaactcc aagtcacat ccttggaac tggggacttg cgcaggtag ccttgaggat 120  
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtta ccgccaatga tgaacacatt 240  
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 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

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 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180  
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tcaactgaaa tctggctaata 240  
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
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 cctagaagtt acagagcatc tagctggtgc gctggcacc ctaggctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctggttagca attctatgcg 240  
 taaaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300  
 c 301

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 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
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 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240  
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctctcgtcagt atagtcttc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

<400> 235  
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 aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg 120  
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata 180  
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca 240  
 ttagggattc aaagaaatat tagatttaag ctacactgg tca 283

<210> 236  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 236  
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 tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggatatag 180  
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240  
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300  
 a 301

<210> 237  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 237  
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 actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg 120  
 ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatect 180  
 ttgggtagtt ggtgccaagc tcttcaatgg cacagaatgg atcagcttct cgtaaatacta 240  
 gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcttttctc 300  
 t 301

<210> 238  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 238  
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 gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca 120  
 ccttgagact tccggagtcg aggccttcca gggttcccca gcccatcaat cattttctgc 180  
 acccccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240  
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300  
 t 301

<210> 239  
 <211> 239  
 <212> DNA  
 <213> Homo sapien

<400> 239  
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 cataatacct tagagatcaa gaaacattta cacagttaa ctgtttaaaa atagctcaac 180  
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<210> 240

<211> 300  
 <212> DNA  
 <213> Homo sapien

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 gggatctgcc ctccagtggg acctttttaag gaagaagtgg gccaagcta agttccacat 120  
 gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg 180  
 ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac 240  
 gctgtgggtg tactttgatg aaaataccca ctttggtggc ctttctgaag ctataatgtc 300

<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241  
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 ctctccatg tattggaaaa ctgcaaaactg gactcaactg gaaggaagtg ctgctgccag 180  
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240  
 tcctctcct gtcatacggc ctctctcaag catcctttgt tgcaggggc ctaaaaggga 300  
 g 301

<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242  
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 gtcttcaaga atatatacatt cttttttcac tagaaccat tcaaaatata agtcaagaat 180  
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240  
 taagtaccca aagttttata aatcaaaagc cctaatagata accattttta gaattcaatc 300  
 a 301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 243  
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 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcgcatga tgaccagcgt 180  
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccg 240  
 tcactaccgc atgttccaga aaggacagga gacgtccacc aatccattg cttccatttt 300  
 t 301

<210> 244  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 244  
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 gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120

ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa 180  
 aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca 240  
 actgtttgtc ttttgtgtat cttttttaa ctgtaaagtt caattgtgaa aatgaatatc 300

<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

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 tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120  
 aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat 180  
 gttttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240  
 agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa 300  
 g 301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

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 agtgcttctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180  
 taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240  
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<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

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 gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180  
 ccttgatgat caagggtggg gcttaagtgg attaaggag gcaagttctg ggttccttgc 240  
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 a 301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

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 acaggaagaa agtggttgg aagacagcca aagaaataaa agcagattaa attgtatcag 180  
 gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag 240  
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 c 301

<210> 249

<211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 249

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ccagggagac	acagcagtga	ctcagagctg	gtcgcacact	gtgcctccct	cctcaccgcc	180
catcgtaatg	aattattttg	aaaattaatt	ccaccatcct	ttcagattct	ggatggaaag	240
actgaatctt	tgactcagaa	ttgtttgctg	aaaagaatga	tgtgactttc	ttagtcattt	300
a						301

&lt;210&gt; 250

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 250

ggtctgtgac	aaggacttgc	aggctgtggg	aggcaagtga	cccttaacac	tacacttctc	60
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cataagcaca	tcagtacttt	tctctggctg	gaatagtaaa	ctaaagtatg	gtacatctac	180
ctaaaagact	actatgtgga	ataatacata	ctaatgaagt	attacatgat	ttaaagacta	240
caataaaacc	aaacatgctt	ataacattaa	gaaaaacaat	aaagatacat	gattgaaacc	300
a						301

&lt;210&gt; 251

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 251

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agacaacctc	atagagcata	ggagaactgg	ttgccctggg	ggcaggggga	ctgtctggat	120
ggcaggggtc	ctcaaaaatg	ccactgtcac	tgccaggaaa	tgcttctgag	cagtacacct	180
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cctctggagg	ggggcagtg	aatcccagct	ccaggacgga	tcctgtcgaa	aagatatcct	300
c						301

&lt;210&gt; 252

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 252

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tcattctctt	ttcactagga	acccattcaa	aatataagtc	aagaatctta	atatcaacaa	180
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tttataaatc	aaaagcccta	atgataacca	tttttagaat	tcaatcatca	ctgtagaatc	300
a						301

&lt;210&gt; 253

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 253

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tggctctgatt gttttcagac cttaaaatat aaacttggtt cacaagcttt aatccatgtg 180  
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 <212> DNA  
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 ccaaatctct tcatettacc ctggtggact cctgactgta gaattttttg gttgaaacaa 180  
 gaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc 240  
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 t 301

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 <212> DNA  
 <213> Homo sapien

<400> 255  
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 attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat 120  
 tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg 180  
 aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta 240  
 aacattatta aaaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac 300  
 aa 302

<210> 256  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 256  
 gttccagaaa acattgaagg tggttccca aagtctaact agggataccc cctctagcct 60  
 aggaccttc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc 120  
 acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat 180  
 aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt 240  
 gtggcctctc ggcctgggta gcaagaacat tcagggtagg cctaagttn tcgtgttagt 300  
 t 301

<210> 257  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 257  
 gttgtggagg aactctggct tgctcattaa gtctactga ttttactat cccctgaatt 60  
 tccccactta tttttgtctt tcaactatcgc aggccttaga agaggtctac ctgcctccag 120  
 tcttacctag tccagtctac ccctggagt tagaatggcc atcctgaagt gaaaagtaat 180

```

gtcacattac tcccttcagt gattttcttgt agaagtgcc aatccctgaat gccaccaaga      240
tcttaattctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc      300
c                                                    301

```

&lt;210&gt; 258

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 258

```

cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc      60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc      120
cccaggggcaa caagaatcca ataccaggac tggggcaaat cttcaaagat cttaacactg      180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat      240
tggtgatccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac      300
t                                                    301

```

&lt;210&gt; 259

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 259

```

tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg      60
gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa      120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtggggccag gaaggctctgt      180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttgggctt      240
ccctcccac tcttcaagca gtgtccttgt tgagccattt gcaccccttg ctccagggtgg      300
c                                                    301

```

&lt;210&gt; 260

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 260

```

ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt      60
aagggtgtctt aacttgaaaa agattaggag tcaactggttt acaagttata attgaatgaa      120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacia caggattaac      180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttataaac agactgattc      240
actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca      300
c                                                    301

```

&lt;210&gt; 261

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<400> 261  
 aaatattcga gcaaatcctg taactaatgt gtctccataa aaggttttga actcagtga 60  
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120  
 agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat 180  
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcttag ttaagtgaag 240  
 ggcatgatga tcatccaaag cccagtgggc acttactcca gactttctgc aatgaagatc 300  
 a 301

<210> 262  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 262  
 gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaacc ctgagtcacc 120  
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
 gggctttctg gtgcacacct aattttgtgc atctttgcc taaatcctgg attagtcccc 240  
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
 c 301

<210> 263  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (301)  
 <223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaaatgac tcacaaaact gatttttaaa tcaagttaat gtgaattttg 60  
 aaaattacta cttaaatccta attcacaata acaatggcat taagggttga cttgagttgg 120  
 ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga cttcccagta aggtctctca aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60  
 aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 120  
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240  
 acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcat 300  
 a 301

<210> 265  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265



tgcccaagtt	atgtgtaagt	gtatccgcac	ccagaggtaa	aactacactg	tcattcttgg	60
cttcttgtga	cgcagtattt	cttctctggg	gagaagccgg	gaagtcttct	cctggctcta	120
catattcttg	gaagtctcta	atcaactttt	gttccatttg	tttcatttct	tcaggaggga	180
ttttcagttt	gtcaacatgt	tctctaacaa	cacttgccca	tttctgtaaa	gaatccaaag	240
cagtcgaagg	ctttgacatg	tcaacaacca	gcataactag	agtatccttc	agagatacgg	300
c						301

&lt;210&gt; 266

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 266

taccgtctgc	ccttctctcc	atccaggcca	tctgcgaate	tacatgggtc	ctcctattcg	60
acaccagatc	actcttttct	ctaccacacag	gcttgctatg	agcaagagac	acaacctctc	120
ctcttctgtg	ttccagcttc	ttttctgtgt	cttccacccc	cttaagttct	attcctgggg	180
atagagacac	caatacccat	aacctctctc	ctaagcctcc	ttataaccca	gggtgcacag	240
cacagactcc	tgacaactgg	taaggccaat	gaactgggag	ctcacagctg	gctgtgcctg	300
a						301

&lt;210&gt; 267

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 267

aaagagcaca	ggccagctca	gcctgccctg	gccatctaga	ctcagcctgg	ctccatgggg	60
gttctcagtg	ctgagtcctc	ccaggaaaag	ctcacctaga	ccttctgagg	ctgaatcttc	120
atcctcacag	gcagcttctg	agagcctgat	attcctagcc	ttgatgggtc	ggagtaaagc	180
ctcattctga	ttcctctctc	tcttttcttt	caagttggct	ttcctcacat	ccctctgttc	240
aattcgcttc	agcttgtctg	cttttagcct	catttccaga	agcttcttct	ctttggcatc	300
t						301

&lt;210&gt; 268

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 268

aatgtctcac	tcaactactt	cccagcctac	cgtggcctaa	ttctgggagt	tttcttctta	60
gatcttgagg	gagctgggtc	ttctaaggag	aaggagggaag	gacagatgta	actttggatc	120
tcgaagagga	agtctaattg	aagtaattag	tcaacggtcc	ttgttttagac	tcttggaata	180
tgctgggtgg	ctcagtgagc	ccttttgagg	aaagcaagta	ttattcttaa	ggagtaacca	240
cttccattg	ttctactttc	taccatcatc	aattgtatat	tatgtattct	ttggagaact	300
a						301

&lt;210&gt; 269

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 269

taacaatata	cactagctat	ctttttaact	gtccatcatt	agcaccaatg	aagattcaat	60
aaaattacct	ttattcacac	atctcaaaac	aattctgcaa	attcttagtg	aagtttaact	120
atagtcacag	accttaata	ttcacattgt	tttctatgtc	tactgaaaat	aagttcacta	180
cttttctgga	tattctttac	aaaatcttat	taaaattcct	ggtattatca	cccccaatta	240
tacagtagca	caaccacctt	atgtagtgtt	tacatgatag	ctctgtagaa	gtttcacatc	300
t						301

<210> 270  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 270  
 cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60  
 cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120  
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180  
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240  
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300  
 a 301

<210> 271  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 271  
 aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60  
 tttatagctc atctttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120  
 gaattgcaat cacttcatca gcctgtatc gctccaatc tctataaagt gggccaagg 180  
 tgaaccacag agccacagca cacctcttcc ccttggtgac tgccttcacc ccatganggt 240  
 tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300  
 c 301

<210> 272  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 272  
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcaactgct tcaaatgctc 60  
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
 tccaataatt cctcatgat gagcaagaaa aattctttgc gcaccctcc tgcattccaca 180  
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgtttcc 240  
 ctaaggactt ccattgcatc tctacaata ttttctctac gcaccactag aattaagcag 300  
 g 301

<210> 273  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 273  
 acatgtgtgt atgtgtatct ttgggaaan aanaagacat cttgtttayt atttttttgg 60  
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa 120

gaaccgtcta	aaaataaaat	ttaccatgtc	dtatatctct	tatagtatgc	ttatttcacc	180
ttytttctgt	ccagagagag	tatcagtgac	ananatttma	gggtgaamac	atgmattggt	240
gggacttnty	tttaengagm	accctgcccc	sgcgccctcg	makcngantt	ccgcsananc	300
t						301

&lt;210&gt; 274

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 274

cttatatact	ctttctcaga	ggcaaaagag	gagatgggta	atgtagacaa	ttctttgagg	60
aacagtaa	gattattaga	gagaangaat	ggaccaagga	gacagaaatt	aacttgtaaa	120
tgattctctt	tggaatctga	atgagatcaa	gaggccagct	ttagcttggt	gaaaagtcca	180
tctaggtatg	gttgcatctt	cgtcttcttt	tctgcagtag	ataatgaggt	aaccgaaggc	240
aattgtgctt	cttttgataa	gaagctttct	tggtcatatc	aggaaattcc	aganaaaagtc	300
c						301

&lt;210&gt; 275

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 275

tcggtgtcag	cagcacgtgg	cattgaacat	tgcaatgtgg	agcccaaacc	acagaaaatg	60
gggtgaaatt	ggccaacttt	ctattaactt	atggtggcaa	ttttgccacc	aacagtaagc	120
tggtcccttct	aataaaagaa	aattgaaagg	tttctcacta	aacggaatta	agtagtggag	180
tcaagagact	cccaggcctc	agcgtacctg	cccgggcggc	cgctcgaagc	cgaattctgc	240
agatatccat	cacactggcg	gncgctcgan	catgcatcta	gaaggnccaa	ttcgccctat	300
a						301

&lt;210&gt; 276

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 276

tgtacacata	ctcaataaat	aaatgactgc	atttgtggtat	tattactata	ctgattatat	60
ttatcatgtg	acttctaatt	agaaaatgta	tccaaaagca	aaacagcaga	tatacaaaat	120
taaagagaca	gaagatagac	attaacagat	aaggcaactt	atacattgag	aatccaaatc	180
caatacat	tttgaacatt	gaaatgaggg	ggacaaatgg	aagccagatc	aaatttgtgt	240
aaaactattc	agtatgtttc	ccttgcttca	tgtctgagaa	ggctctcctt	caatggggat	300
g						301

&lt;210&gt; 277

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccc cctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtcntccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgta 120  
 cagtccttac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgc 180  
 aatgaacatc tcagtgtgct tcacaatgtt ctggcactat tataagtgtc tcacaggttt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttttctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaaagggt gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa	acctaagatt	agcccaggta	gttgccctgta	acttcagttt	ttctgcctgg	180
gtttgatata	gtttagggtt	ggggtttagat	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtatgttcc	atgtttattt	gttaaagcag	300
t						301

&lt;210&gt; 281

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 281

aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatatcc	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcttta	tcgggttata	cggatgagaa	gaactccctt	tgagagagaa	180
tgtgtagcac	actgcgatta	cagctaaata	acccgtattt	gtgtgtcatg	tttgcatttc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagtt	gcagtacctc	300
g						301

&lt;210&gt; 282

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 282

caggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaacct	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagccag	gcagaacct	gctaacctta	cagctcagcc	tgacacagaag	180
cgcagaagca	aagcccaggc	agaacctatg	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gcccaggcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

&lt;210&gt; 283

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 283

atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttggt	aaattctata	atggtgatat	gcattcttta	240
ggaaacatat	acatttttaa	aaatctattt	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

&lt;210&gt; 284

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 284

caggtacaaa	acgtatttaa	gtggcttaga	atgtgaacat	ttgtggctctt	tatttacttt	60
gcttcgtgtg	tgaggcaaag	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaagggg	gctgacctgg	agcagagcat	180
ggtgagaggc	aaggcatgag	agggcaagtt	tggtgtggac	agatctgtgc	ctactttatt	240
actggagtaa	aagaaaacaa	agttcattga	tgtcgaagga	tatatacagt	gttagaaatt	300
a						301

&lt;210&gt; 285

<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 285  
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
attaaatatg tctgacttct tttgaggtca cagcactagg caaatgctat ttacgatctg 240  
caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300  
t 301

<210> 286  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 286  
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60  
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180  
aaaataagct accatatagc ttataagtct caaattttgg ctttttacta aaatgtgatt 240  
gtttctgttc attgtgtatg cttcatcacc tatattaggg aaattccatt ttttcccttg 300  
t 301

<210> 287  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 287  
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg 120  
aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180  
ccgtgggtat ctccctccca gcttggctgc ctcagtgtat cacagtattc cattttgttt 240  
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300  
t 301

<210> 288  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 288  
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120  
gatctttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180  
aaaagcatct gcttttgtga ttttaatttag ctcactctgg cactggaaga atccaaacag 240  
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 289  
 ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgtccc tggaaactta 60  
 gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
 ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180  
 cgttctataa atgaatgtgc tgaagcaaag tgcccatggg ggcggcgaan aagagaaaga 240  
 tgtgttttgt tttggactct ctgtgggtccc ttccaatgct gtgggtttcc aaccagnnga 300  
 a 301

<210> 290  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 290  
 acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60  
 tgactgatct gttcatttct ctcacagctc ttaccccaa aagcttttcc accctaagtg 120  
 ttctgacctc ctttttcta ctcacagctc atagaggcag anccacctac aatgaacatg 180  
 gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc 240  
 tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtga 300  
 a 301

<210> 291  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 291  
 caggtacca tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac 60  
 tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120  
 tttactcttt tggttatagg tgaatcaca aatgtatttt tatgtattct gtagttcaat 180  
 agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa 240  
 acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct 300  
 a 301

<210> 292  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 292

```

accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aattttttaag tttaaaagat aaaataccat catttttaaat gttggtattc      120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc      240
tactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                                   301

```

&lt;210&gt; 293

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 293

```

ggtaccaagt gctggtgccg gctgtttacc tgtttctcact gaaaagtctg gctaattgctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt      120
aacacaaacy tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgtttctgt      180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctggg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gtcgagcat      300
g                                                                                   301

```

&lt;210&gt; 294

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 294

```

tgaccataaa caatatacac tagctatctt ttttaactgtc catcattagc accaatgaag      60
attcaataaaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag      120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc      240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt      300
t                                                                                   301

```

&lt;210&gt; 295

&lt;211&gt; 305

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 295

```

gtactctttc tctccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccattcttga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt      240
tctcagaacc atttcaccca gacagcctgt ttctatcttg ttttaataaat tagtttgggt      300
tctct                                                                                   305

```

&lt;210&gt; 296

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 296

```

aggtagctatg ggaagctgct aaaataatat ttgatagtaa aagtagttaa tgtgctatct      60

```



```

cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg      120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac      180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt      240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg      300
c                                                                    301

```

<210> 297

<211> 300

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (300)

<223> n = A,T,C or G

<400> 297

```

actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttggtgcta      60
aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga      120
acaaaganagt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt      180
tccatcattg ggagtgcact ggccatccct caaaatttgc ctgggctggc ctgagtgggc      240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg      300

```

<210> 298

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (301)

<223> n = A,T,C or G

<400> 298

```

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg      60
ggcatctgag agacctgggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg      120
tgaagctctc agatcaatca cggaaggggc ctggcggttg tggccacctg gaaccaccct      180
gtcctgtctg ttacatttc actaycaggt tttctctggg cattacnatt tgttccccta      240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcagggtggct ctacagcgagg      300
t                                                                    301

```

<210> 299

<211> 301

<212> DNA

<213> Homo sapien

<400> 299

```

gttttgagac ggagtttcac tcttggtgcc cagactggac tgcaatggca gggctctctgc      60
tcaactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct ccaggttagc      120
tggtattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg      180
gagtttcgcc atgttggtgca gctgggtctca aactcctgac ctcaagcgac ctgcctgcct      240
cggcctccca aagtgtctgga attataggca tgagtcaaca cgcccagcct aaagatatatt      300
t                                                                    301

```

<210> 300

<211> 301

<212> DNA

<213> Homo sapien

&lt;400&gt; 300

```

attcagtttt atttgcgtgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga      60
tatgtccac acccactggg aaaggctccc acctggctac ttctctatc agctgggtca      120
gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta      180
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac      240
tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat      300
g                                                                                   301

```

&lt;210&gt; 301

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 301

```

ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc      60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt      120
gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaagacc      180
ctcagagctg agacaccac aacagtggga gctcacaaag accctcagag ctgagacacc      240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt      300
t                                                                                   301

```

&lt;210&gt; 302

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 302

```

aggtacacat ttagcttggt gtaaatgact cacaaaactg attttaaaat caagttaatg      60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac      120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg      180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca      240
caggatttga gatgctaagg ccccagagat cgtttgatcc aacctcttta ttttcagagg      300
g                                                                                   301

```

&lt;210&gt; 303

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 303

```

aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt      60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac      120
tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc      180
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc      240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac      300
c                                                                                   301

```

&lt;210&gt; 304

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 304

```

acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaata      60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc      120
cttttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctgggtgcagt      180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga      240

```

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300  
c 301

<210> 305  
<211> 301  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 305  
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60  
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg 120  
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180  
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa 240  
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
a 301

<210> 306  
<211> 8  
<212> PRT  
<213> Homo sapien

<400> 306  
Val Leu Gly Trp Val Ala Glu Leu  
1 5

<210> 307  
<211> 637  
<212> DNA  
<213> Homo sapien

<400> 307  
acaggggratg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttgggtcc 60  
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac 120  
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttatct gccttmtttt 180  
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatggtt gaacacccca 240  
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300  
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360  
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacgggtggg caaactctga 420  
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagttaa 480  
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca 540  
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600  
ttacagatac tggggcagca aataaaactg aatctttg 637

<210> 308  
<211> 647  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n = A,T,C or G

&lt;400&gt; 308

acgattttca	ttatcatgta	aatcgggtca	ctcaaggggc	caaccacagc	tgggagccac	60
tgctcagggg	aaggttcata	tgggactttc	tactgcccac	ggttctatac	aggatataaa	120
ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
ccaccctctc	gaccctttgg	aactcctctg	acccttttaga	acaagcctac	ctaatatctg	240
ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
cttggttaag	atgtgggttc	cacattaggt	tctgaatatg	gggggaaggg	tcaatttgct	360
cattttgtgt	gtggataaag	tcaggatgcc	caggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gccatgaaga	cttgaggggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggcaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
aatgtccttt	tttttctcct	gcttctgact	tgataaaaagg	ggaccgt		647

&lt;210&gt; 309

&lt;211&gt; 460

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 309

actttatagt	ttaggctgga	cattgaaaa	aaaaaaaaagc	cagaacaaca	tgtgatagat	60
aatatgattg	gctgcacact	tccagactga	tgaatgatga	acgtgatgga	ctattgtatg	120
gagcacatct	tcagcaagag	ggggaaatac	tcattcatctt	tggccagcag	ttgtttgatc	180
accaaacatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtcag	240
ggggaattta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctaccag	300
ctgggggtgt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggtaacc	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

&lt;210&gt; 310

&lt;211&gt; 539

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 310

acgggactta	tcaataaaag	ataggaaaag	aagaaaactc	aaatattata	ggcagaaatg	60
ctaaaagggtt	taaaatatgt	caggattgga	agaaggcatg	gataaagaac	aaagttcagt	120
taggaaagag	aaacacagaa	ggaagagaca	caataaaaagt	cattatgtat	tctgtgagaa	180
gtcagacagt	aagatttgtg	ggaaatgggt	tggtttgttg	tatggtagat	attttagcaa	240
taatctttat	ggcagagaaa	gctaaaatcc	tttagcttgc	gtgaatgatc	acttgctgaa	300
ttcctcaagg	taggcatgat	gaaggagggt	ttagaggaga	cacagacaca	atgaactgac	360
ctagatagaa	agccttagta	tactcagcta	ggaatagtga	ttctgagggc	acactgtgac	420
atgattatgt	cattacatgt	atggtagtga	tggggatgat	aggaagggaag	aacttatggc	480
atattttcac	ccccacaaaa	gtcagttaaa	tattgggaca	ctaaccatcc	aggtcaaga	539

&lt;210&gt; 311

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(526)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 311

caaatttgag	ccaatgacat	agaattttac	aaatcaagaa	gcttattctg	gggccatttc	60
ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaaatg	tggttcagcat	gaaatattag	ctacagggga	agctaataaa	180

attaaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggtctgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atccccaag	cacagt		526

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 312

cctctctctc	cccacccct	gactctagag	aactgggttt	tctcccagta	ctccagcaat	60
tcattttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccattttctct	ttcccttcca	cctgccagtt	ttgctgactc	tcaacttgtc	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccccctct	300
tgcagatgtc	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaattgtg	gtttcctttg	taaaccanga	ttcttatttg	nctgggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (718)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 313

ggagatttgt	gtggtttgca	gccgaggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgatata	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgcata	gtttttgcac	atttccagcc	cttttaaata	tccacacaca	caggaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccggccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttggtg	gggaaggaca	ttagaaaatg	aattgatgtg	360
ttccttaaa	gatggcagga	aaacagatcc	tggttggtg	atttatttga	acgggattac	420
agatttgaaa	tgaagtcaca	aagtgagcat	taccaatgag	aggaaaacag	acgagaaaat	480
cttgatgggt	cacaagacat	gcaacaaaca	aaatggaata	ctgtgatgac	acgagcagcc	540
aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaataac	tgacttacgg	660
ttcttntggc	ccacattttc	atnateccacc	ccntcntttt	aannttantc	caaantgt	718

&lt;210&gt; 314

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

gtttattttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata 60  
cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg 120  
caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180  
gctctcggta gtccagccac tgtgaaacat gtcaccttta gattaacctc gtggacgctc 240  
ttgttgattt gctgaactgt agtgcctgtt attttgcttc tgtctgtgaa ttctgttgct 300  
tctggggcat ttccttggtga tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315  
<211> 341  
<212> DNA  
<213> Homo sapien

<400> 315  
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gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180  
agtcaccagc tccccgacca gccggatata gtccttaggg gtcattgtagg cttcctgaag 240  
tagcttctgc tgtaagaggg tgttgctccg ggggctcgtg cggttattgg tcctgggctt 300  
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<210> 316  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 316  
agactgggca agactcttac gcccacact gcaatttggt cttgttgccg tatccattta 60  
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cattcagggg gctctggttg caatattagt t 151

<210> 317  
<211> 151  
<212> DNA  
<213> Homo sapien

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ccagggctct gttcttgcca cactgcttg a 151

<210> 318  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 318  
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<210> 319  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 319  
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taagattggg tttatgtgat tttagtgggt a 151

<210> 320  
<211> 150  
<212> DNA  
<213> Homo sapien

<400> 320  
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<210> 321  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 321  
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tgcctctgag aaatcaaagt cttcatacac t 151

<210> 322  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 322  
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tttgggcttg gtcagtttg cacagggtt ggagatggtg acagtcttct ggcattcggc 120  
attgtgcagg gctcgttca nacttcagt t 151

<210> 323  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 323  
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nagactcant tactaccag tttgtggtt twtgggagaa atgtaactgg acagttagct 120  
gttcaatyaa aaagacactt anccatgtg g 151

<210> 324  
<211> 461  
<212> DNA  
<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(461)  
 <223> n = A,T,C or G

<400> 324  
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 agaagtgggtc agctaaagga atccagggtg ttgggtggac tgtaataacc ttgatgaaa 120  
 agagttacta cgaatcccat cttgggtcca gctatatcac tgacagcatg gtagaagact 180  
 gcgaacctca cttctagact ttcacgggtg gacgaaacgg gttcagaaac tgccaggggc 240  
 ctcatacagg gatatcaaaa taccctttgt gctaccagg ccctggggaa tcagggtgact 300  
 cacacaaatg caatagttgg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt 360  
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 aaaaacgcac aagagcccct gccctgccct agctgangca c 461

<210> 325  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

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 <211> 1215  
 <212> DNA  
 <213> Homo sapien

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<210> 327  
 <211> 220



&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 327

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Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
 1          5          10          15
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
          20          25          30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
          35          40          45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
          50          55          60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65          70          75          80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
          85          90          95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
          100          105          110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
          115          120          125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
          130          135          140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145          150          155          160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
          165          170          175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
          180          185          190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
          195          200          205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
          210          215          220

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&lt;210&gt; 328

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 328

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cgctcgctc tggtagetgc agccaaatca taaacggcga ggactgcagc ccgcaactgc      60
agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc gtcctgggtgc      120
atccgcagtg ggtgctgtca gccacacact gtttccagaa ctctacacc atcgggctgg      180
gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca      234

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&lt;210&gt; 329

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 329

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Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
 1          5          10          15
Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
          20          25          30
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
          35          40          45
His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
          50          55          60

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Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala  
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<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330  
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 gctgcagcca 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331  
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 1 5 10 15  
 Val Ser Gly Ser Cys Ser  
 20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332  
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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&lt;210&gt; 334

&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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&lt;210&gt; 335

&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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 <211> 147  
 <212> PRT  
 <213> Homo sapien

<400> 336  
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 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln  
 35 40 45  
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala  
 50 55 60  
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln  
 65 70 75 80  
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln  
 85 90 95  
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala  
 100 105 110  
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn  
 115 120 125  
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro  
 130 135 140  
 Ala Phe Trp  
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<210> 337  
 <211> 9  
 <212> PRT  
 <213> Homo sapien

<400> 337  
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<210> 338  
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 <212> PRT  
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<400> 338  
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 <212> PRT  
 <213> Homo sapien

<400> 339  
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<211> 483
<212> DNA
<213> Homo sapien
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<211> 344
<212> DNA
<213> Homo sapien
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attaatttaa taatttctga tgatgggttt atctgcagta atatgtatat catctattag	240
aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc	300
ctgattctta acattgtctt taatgaccac aagacaacca acag	344

&lt;210&gt; 342

&lt;211&gt; 592

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 342

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cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg	180
accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact	240
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cccgtgtcct tatgcaaata atcgtcttct tctaaatttc tcctaggctt cattttccaa	480
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&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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aaaccaccaa gctgaaaaaa aa	382

&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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&lt;210&gt; 345

&lt;211&gt; 251



<212> DNA

<213> Homo sapien

<400> 345

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gcgtgggcca	ggaaatcaca	tcctacactg	cccaggagcc	agacacattt	atggaacaga	180
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<210> 346

<211> 282

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(282)

<223> n = A,T,C or G

<400> 346

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aggagacta	tacctggctc	ttgccctaag	tgagaggtct	tccctcccgc	accaaaaaat	180
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<210> 347

<211> 201

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

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<223> n = A,T,C or G

<400> 347

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tctgagactg	actggacceca	cccagacceca	gggcaaagat	acatgttacc	atatcatctt	180
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<210> 348

<211> 251

<212> DNA

<213> Homo sapien

<400> 348

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aggagacact	cccagcatgg	aggagggttt	atcttttcat	cctaggtcag	gtctacaatg	180
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gccctgcctc	c					251

<210> 349

<211> 251

<212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

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cagaaggggc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca	240
actcctgggtt t	251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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aatcgacg	908

&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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gtaatatata tttagggag atgttgcttt gccacacac gaagcaaagt aa	472

&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

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caggctcgt tccgtcctta cgatgaagac cacgatgcag tttccaaaca ttgccactac	180
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 <212> DNA  
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<210> 354  
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 <212> DNA  
 <213> Homo sapien

<400> 354  
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 caatatggaa ggctctaatt tgcccatatt tgaaataata attcagcttt ttgtaataca 660  
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<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355  
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 gcttaaaagaa aaccag 676

<210> 356

<211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356  
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 <211> 393  
 <212> DNA  
 <213> Homo sapien

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 araarataag tggtatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300  
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 <212> DNA  
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 <211> 620  
 <212> DNA  
 <213> Homo sapien

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&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

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&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

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&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

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&lt;210&gt; 363

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 363

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&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

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&lt;210&gt; 365

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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&lt;210&gt; 368

&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 2184

&lt;212&gt; DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 370

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tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat      240
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ctgcggcagc ttccggataa cttgaggctg catcactggg gaagaaacac aytctgttcc      360
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg      420
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&lt;210&gt; 371

&lt;211&gt; 1855

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1855)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 371

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&lt;210&gt; 372

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;210&gt; 373

&lt;211&gt; 1155

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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------------	------------	------------	------------	------------	------------	----

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&lt;210&gt; 374

&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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 <212> DNA  
 <213> Homo sapien

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 <211> 329  
 <212> PRT  
 <213> Homo sapien

<400> 376  
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 20 25 30  
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser  
 35 40 45  
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg  
 50 55 60

```

Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65          70          75          80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
          85          90          95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
          100          105          110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
          115          120          125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
          130          135          140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145          150          155          160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
          165          170          175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
          180          185          190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
          195          200          205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
210          215          220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225          230          235          240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
          245          250          255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
          260          265          270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
          275          280          285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
290          295          300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305          310          315          320
Ser Met Leu Phe Leu Val Ile Ile Met
          325

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&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

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Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
          35          40          45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
50          55          60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65          70          75          80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
          85          90          95

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125

Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
                   100                  105                  110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
                   115                  120                  125  
 Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
                   130                  135                  140  
 Lys Asn Lys Val  
 145

<210> 378  
 <211> 1719  
 <212> PRT  
 <213> Homo sapien

<400> 378  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
   1                  5                  10                  15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
                   20                  25                  30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
                   35                  40                  45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
                   50                  55                  60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
                   65                  70                  75                  80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
                   85                  90                  95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
                   100                  105                  110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
                   115                  120                  125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
                   130                  135                  140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
                   145                  150                  155                  160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
                   165                  170                  175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
                   180                  185                  190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
                   195                  200                  205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
                   210                  215                  220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
                   225                  230                  235                  240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
                   245                  250                  255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
                   260                  265                  270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
                   275                  280                  285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
                   290                  295                  300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
                   305                  310                  315                  320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
                   325                  330                  335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val



805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230  
 Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro



1265		1270		1275		1280
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr						
	1285			1290		1295
Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp						
	1300			1305		1310
Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val						
	1315			1320		1325
His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala						
	1330			1335		1340
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala						
1345		1350		1355		1360
Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn						
	1365			1370		1375
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr						
	1380			1385		1390
Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr						
	1395			1400		1405
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu						
	1410			1415		1420
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly						
1425		1430		1435		1440
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn						
	1445			1450		1455
Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser						
	1460			1465		1470
Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly						
	1475			1480		1485
Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu						
	1490			1495		1500
Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys						
1505		1510		1515		1520
Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser						
	1525			1530		1535
Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu						
	1540			1545		1550
Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser						
	1555			1560		1565
Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe						
	1570			1575		1580
Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe						
1585		1590		1595		1600
Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly						
	1605			1610		1615
Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro						
	1620			1625		1630
Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln						
	1635			1640		1645
Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile						
	1650			1655		1660
Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser						
1665		1670		1675		1680
Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn						
	1685			1690		1695
Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr						
	1700			1705		1710
Met Lys His Gln Ser Gln Leu						
	1715					

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
                   420                  425                  430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
                   435                  440                  445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
                   450                  455                  460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465                  470                  475                  480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
                   485                  490                  495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
                   500                  505                  510  
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys  
                   515                  520                  525  
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly  
                   530                  535                  540  
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser  
 545                  550                  555                  560  
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr  
                   565                  570                  575  
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln  
                   580                  585                  590  
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln  
                   595                  600                  605  
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys  
                   610                  615                  620  
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile  
 625                  630                  635                  640  
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
                   645                  650                  655

&lt;210&gt; 380

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1                  5                  10                  15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
                   20                  25                  30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
                   35                  40                  45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
                   50                  55                  60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65                  70                  75                  80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
                   85                  90                  95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
                   100                  105                  110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
                   115                  120                  125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
                   130                  135                  140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145                  150                  155                  160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415  
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp  
 515 520 525  
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys  
 530 535 540  
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala  
 545 550 555 560  
 Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg  
 565 570 575  
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His  
 580 585 590  
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys

625		630		635		640
Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala						
		645		650		655
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu						
	660		665		670	

&lt;210&gt; 381

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 381

ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa	60
ggtaacatgc ttcccctaag ggtatcccaa cccaggggccc tcaccatgac ctctgagggg	120
ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggaccca ggactcacac	180
atcctggggc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa	240
caagcagtca g	251

&lt;210&gt; 382

&lt;211&gt; 3279

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 382

cttcctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa	60
atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt	120
caactggagg ggacatcctg cagaaggtag gagtgcagaa acacccgctg caggggaggg	180
gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggagggg	240
gggcctggag ggcgtgagga ggagcgagg ggctgcattg ctggagttag ggatcagggg	300
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gccacaggag gacactgctt ttctctgag gagtgcagg ctgtggatgg tgcaggacag	420
aagaaggaca gggcctggct cagggtgtcca gaggtgtctg ctggcttccc tttgggatca	480
gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg	540
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ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca	780
gcactctgca gatgggtccc gccctcatcc tgctgacctg tctgcaggga ctgtcctcct	840
ggaccttgcc ccttgtgcag gactgcagg ctgaagtccc ctcccatag gccaaagactg	900
gagccttgtt cctctgtgtg gactccctgc ccatattctt gtgggagtgg gttctggaga	960
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atcatggggc cctgagccat gtgcccctgc tgaaggcct gctgtgtaca ccaagggtgt	1200
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cccctacctc tagtaaatct aagtcacact cacgttctgg catcacttgg cctttctgga	1320
tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gactcctact	1380
gacctgtgct ttctggtgtg gactccaggg ctgctaggaa aaggaatggg cagacacagg	1440
tgtatgccaa ttttctgaa atgggtataa ttctgctcct tccttcggaa cactggctgt	1500
ctctgaagac ttctcgtca gtttcagtga ggcacacac aaagacgtgg gtgacctgt	1560
tgtttgtggg gtgcagagat gggaggggtg gggcccaccc tggagagtg gacagtga	1620
caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac	1680
acacacagca aggttgacgc tgtaaacata gccacgctg tcctgggggc actgggaagc	1740
ctagataagg ccgtgagcag aaagaagggg aggatectcc tatgttgttg aaggagggac	1800
tagggggaga aactgaaagc tgattaatta caggaggttt gttcagggtcc cccaaaccac	1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt	1920
ttattatggg ttgttacatt gataggatac atactgaaat cagcaacaa aacagatgta	1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc	2040

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tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgatac cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcataatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
caaggatgta tgataaatatg tacaagtaaa ttccaactga ggaagctcac ctgaccccta 2280
gtgtccaggg tttttactgg gggctctgtag gacgagtatg gactacttga ataattgacc 2340
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gcagggtctgc tgagtcaacc ttttattgta caggggatga gggaaaggga gaggatgagg 2640
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aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
atcattgttt tatttgctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca cccacacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
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cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaataaaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

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&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

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Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5                                10                    15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                                25                    30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                                40                    45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                                55                    60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                                70                    75                    80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                                90                    95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                               105                    110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                               120                    125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                               135                    140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                               150

```

<210> 384  
 <211> 557  
 <212> DNA  
 <213> Homo sapiens

<400> 384  
 ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
 aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120  
 ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggg 180  
 tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240  
 acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300  
 ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360  
 tccccaaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420  
 cttctttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
 tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540  
 aaaaaaaaaa aaaaaaa 557

<210> 385  
 <211> 337  
 <212> DNA  
 <213> Homo sapiens

<400> 385  
 ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60  
 gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
 tctcaaagcc atctgctgtc ttcgagtaag gacacatcat cactcctgca ttgttgatca 180  
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
 tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgctcgtg gtctggatct 300  
 ctttggccac caattcccc ttttccacat cccggca 337

<210> 386  
 <211> 300  
 <212> DNA  
 <213> Homo sapiens

<400> 386  
 gggcccgtcta ccggcccagg cccgcctcgc cgagtctctc tccccgggtg cctgcccgcga 60  
 gccgcgtcgg ccagaggggt gggcgcgggg ctgcctctac cggttgccgg ctgtaactca 120  
 gcgaccttgg ccgaaggct ctacgaagga cccaccgacc ccagccgcgg cggcggcggc 180  
 gcggaactttg cccggtgtgt ggggcgggagc ggactgctgt tccgcggacg ggcagcgaag 240  
 atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
 <211> 537  
 <212> DNA  
 <213> Homo sapiens

<400> 387  
 gggccgagtc gggcaccaag ggactctttg caggcttctt tcctcggtac atcaaggctg 60  
 cccctcctcg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120  
 tgaaccagga ccggcttctg ggcggctgaa aggggcaagg aggaaggac cccgtctctc 180  
 ccacggatgg ggagagggca ggaggagacc cagccaagt ccttttctc agcactgagg 240  
 gagggggcct gtttcccttc cctcccggcg acaagctcca gggcagggt gtccctctgg 300  
 ggggcccagc acttctctag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360  
 cttaccacc ccccaagttc aagaccaaata ctccagctg ccccttctgt gtttccctgt 420  
 gtttgcgtga gctgggcatg tctccaggaa ccaagaagcc ctacgcctgg tgtagtctcc 480  
 ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaaa aaaaaaa 537

<210> 388  
 <211> 520  
 <212> DNA  
 <213> Homo sapiens

<400> 388  
 aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60  
 tgagggttaaa ccagtttgca ttcccctaata gtggaaaaag taagaggact actcagcact 120  
 gtttgaagat tgccctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180  
 ggacccccctc cccaacatgc cccagccccc ccctaagcat ggtcccttgt caccaggcaa 240  
 ccaggaaaact gctacttgtg gacctcacca gagaccagga ggggtttggt agctcacagg 300  
 acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360  
 tcataactcaa ttgatgggta ttagacaatt ccatttcttt ctgggtatta taaacagaaa 420  
 atctttctctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480  
 atgaacttgt cttattttta tgggtgggtt ttttctggt 520

<210> 389  
 <211> 365  
 <212> DNA  
 <213> Homo sapiens

<400> 389  
 cgttgccccca gtttgacaga aggaaaggcg gagcttatcc aaagtctaga gggagtggag 60  
 gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120  
 aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180  
 aagcctatgg ccagctgtct ttgtgttccc tctcacccgc ctgtcctcac agctgagact 240  
 cccaggaaac cttcagacta ccttctctctg ccttcagcaa ggggcgttgc ccacattctc 300  
 tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360  
 gggag 365

<210> 390  
 <211> 221  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(221)  
 <223> n = A,T,C or G

<400> 390  
 tgccctctcca tcttggtccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60  
 tacacggntt ctcatgggtg tggaacatct ctgcttgccg ttccaggaag gcctctggct 120  
 gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180  
 tcaaagtcta gaggagtggt aggagttaag gctggatttc a 221

<210> 391  
 <211> 325  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(325)  
 <223> n = A,T,C or G

<400> 391



```

tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgcag tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc                                     325

```

```

<210> 392
<211> 277
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(277)
<223> n = A,T,C or G

```

```

<400> 392
atattgttta actccttcct ttatatcttt taacattttc atggngaaaag gttcacatct 60
agtctcactt nggnagnngn ctctactctg agtctcttcc cgggcctggn ccagtnghaa 120
antaccanga accgncatgn cttaanaacn ncctgggttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatag agcgccgcgt cctgtgttgc tgggggaa                                     277

```

```

<210> 393
<211> 566
<212> DNA
<213> Homo sapiens

```

```

<400> 393
actagtccag tgtggtggaa ttcgcgcccg cgtcgacgga caggtcagct gtctggetca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga tttaaattcag cctaaacggt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggctc agtttgtcca tcagcattat catgatatca ggactgggta cttgggttaag 240
gaggggtcta ggagatctgt cctttttaga gacaccttac ttataatgaa gtatttgga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatatc atatctctac gctggaaact 420
ttctgectca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaaa aaaaaa                                     566

```

```

<210> 394
<211> 384
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(384)
<223> n = A,T,C or G

```

```

<400> 394
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggctggact gctggaagct gtgaaggagc tacaggccna 120
gcaggaggac cgggctttta ggagttttta gctgagtgct actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagc aattacccaa atccggttgg agcatgacgt 240
gaacatccag ttctctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtagcaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

```

tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

```

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctcaactacag acctctgacc atgggacggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac

```

399

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```

tggagtntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc ttagagaaa aaaaggagtt gttagtagat 180
actaaaaaa gtggatgaat aatctggata ttttccctaa aaagattcct tgaaacacat 240
taggaaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gcctgctct ttt

```

403

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```

actagtnacg tgtggtggaa ttgcggccg cgtcgaccta naanccatct ctatagcaaa 60
tccatccccg ctcttggttg gtnacagaat gactgacaaa

```

100

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

```

<400> 398
gcgggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtgggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

```

```

<210> 399
<211> 298
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G

```

```

<400> 399
acggagggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
gggggtgcng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcgtgggct 180
ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcattggg 298

```

```

<210> 400
<211> 548
<212> DNA
<213> Homo sapiens

```

```

<400> 400
acatcaacta cttectcatt ttaaggatg gcagttccct tcatccctt ttctgcctt 60
gtacatgtac atgtatgaaa ttctcttctc ttaccgaact ctctccacac atcacaagg 120
caaagaacca cagccttaga agggtgaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt ttttccacgt ttaaggggccc atggcaggac ttagagttgc gagttaagac 240
tgagaggggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatccc 300
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
gttggtccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggcccc ctctgggat caagcccctc ccaggccctg 480
tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tcccattggg 540
agcaggtt 548

```

```

<210> 401
<211> 355
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(355)
<223> n = A,T,C or G

```

```

<400> 401
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgcc atgggtggcg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnngg tttccaacca ggggaagggt 300

```

```

cccttttgc tgcgaagt ccataacat gagcactact ctaccatggn tctgc      355

<210> 402
<211> 407
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1) ... (407)
<223> n = A,T,C or G

<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca ttccaa      407

<210> 403
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1) ... (303)
<223> n = A,T,C or G

<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacccaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga      303

<210> 404
<211> 225
<212> DNA
<213> Homo sapiens

<400> 404
aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120
acattttcca ctcggttttc catagttggt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt      225

<210> 405
<211> 334
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1) ... (334)

```

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtcct tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gtcacagcc ttctctagge 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

```
tttcatacct aatgaggagg ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaatt 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagt tttaaagaca atgggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

```
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tnccttaacta gttaatcctt aaagggtan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(250)  
<223> n = A,T,C or G

<400> 409  
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60  
gtggttttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120  
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180  
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240  
ggcctntatgc 250

<210> 410  
<211> 306  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(306)  
<223> n = A,T,C or G

<400> 410  
ggctgggttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60  
agtcttgcaa tcccatgtgc aggatccgtc tgtgcacatg cctctgtaga gaggcagatt 120  
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180  
aaggtgttgt aatggtgaaa accgcttctt tctttattgc cccttcttat ttatgtgaac 240  
nactgggttg ctttttttgn atctttttta aactggaaaag ttcaattgng aaaatgaata 300  
tcntgc 306

<210> 411  
<211> 261  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(261)  
<223> n = A,T,C or G

<400> 411  
agagatattn cttaggtnaa agttcataga gtteccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
cttctctcaa ggngaggcaa a 261

<210> 412  
<211> 241  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```
gttcaatggt acctgacatt tctacaacac ccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a                                                                                   241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcatctgtg tgcttgaate ctttccactg tctcatctec 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tctctatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t                   231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggg cttccttttg catgggatgg ggatgaagta aggagagggg 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca          234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggg tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc                                217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

```

<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
atgcataatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                               213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaate ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt                               303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
tttttggcgg tgggtgggga gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac cctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacacca gctagttttt 180
gtatttttag tagagacagg gtttcacccat gttggccagg ctggtctcaa actcctnacc 240
tcagnngtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgtctan gattacaggc cgtgagcc                               328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgcatatg 60

```



```

accctgagc catggactgg agcctgaaag gcagcgtaca cctgctcct gatcttgetg 120
cttgtttct ctctgtggct ccattcatag cacagttgtt gactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcactcgct cccgcaaagtg gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg                                     389

```

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```

gttctctcta actcctgcc aaaaacagctc tctcaacat gagagctgca cccctctctc 60
tggccagggc agcaagcctt agccttggtt tcttggttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtccatttga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgtctatg aaaaacctgg caagcccg                                     408

```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```

gctcaaaaat ctttttactg atnggcattg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggctc tttttgggtc cttcttctcc accacnatac acttgcatgc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctc gg                                     352

```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```

atgccaccat gctggcaatg cagcgggagg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gogatagcaa ggtgccggcg atcgcgggcg cgtcaatcct ggccaaggct agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gtttcttccg ccggtacggc tggcctatga aaattat                                     337

```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature  
<222> (1)...(310)  
<223> n = A,T,C or G

<400> 423  
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60  
aggagaatga ggcctggcct gggagccctg tgctactan aagcncatta gattatccat 120  
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180  
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240  
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300  
tccgagttta 310

<210> 424  
<211> 370  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(370)  
<223> n = A,T,C or G

<400> 424  
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60  
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120  
cactgacaga acaggtcttt tttgggtcct tcttctccac cacgatatac ttgcagtcc 180  
ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240  
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300  
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360  
tccgtcgacg 370

<210> 425  
<211> 216  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(216)  
<223> n = A,T,C or G

<400> 425  
aattgctatn ntttatcttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaata 60  
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120  
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccg 180  
gaggntntca ggaccgctcg atgtntnttg aggagg 216

<210> 426  
<211> 596  
<212> DNA  
<213> Homo sapiens

<400> 426  
cttcagtgga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60  
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccagggt tcgctggcca 120  
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180  
gctgtccttg tatcttgatt aacctaattg ccttcccagc acgactcgga ttcagctgga 240  
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaaggaggca cttcccgtta 300

```

ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaaccaat ttgactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgtggt tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

```

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (107)

<223> n = A,T,C or G

<400> 427

```

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccg 60
cccgaggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

```

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (38)

<223> n = A,T,C or G

<400> 428

```

gaacttcena anaangactt tattcactat tttacatt 38

```

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

```

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcctgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcggt 240
gccttcact tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gtttagagaga tatgcatatc cagggtattt ttgccagggt gtaggagaga 540
ttat 544

```

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (507)

<223> n = A,T,C or G

<400> 430

```
cttatcncaa tggggctccc aaacttggt gtgcagtga aactccggg gaattttgaa 60
gaacactgac acccatcttc cccccgaca ctctgattta attgggtgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccgaaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgagggg gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa
507
```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
392
```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgga gtccagccac tgnгааacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca ttctcttgn atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt
387
```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagag ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtag tctttctctc cctcctctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacctt ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtgc 480
ttta 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgcgcgtca gagcagggtca ctttctgcct tccacgtcct ctttcaagga agccccatgt 60
gggtagcttt caatatcgca gggtcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcgga ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgaccc 240
cttgagagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggggtc 120
agcctcttct ggaattcttc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggtg tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cgggtcaacgt ctgtgcttcg aatataaacc 360
```

tgttcattgt tataggactc attcaagaat ttctatatc tctttcttat atactctcca 420  
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480  
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540  
accaaagtca caaacttcaa ctccttggt agtacacttc ggtctagcca gaaaaaagc 600  
agaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660  
tgttgag 667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60  
acacagccag gtaaggaaaag ctggattggc acactaggac tctaccatac cgggttttgt 120  
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180  
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240  
aggctactct ctatcttcac cctcttgct tctactctct ggcagtcaga cctgtgggag 300  
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggag 360  
cattctctca gggtacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420  
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480  
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540  
tctatttctc aggcactgag ggctgtggg taccttgtgg tgccaaaaca gatcctgttt 600  
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660  
ctgcatcatg tgctctcttg gctgaaaatg acc 693

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ctctgtgact 60  
ttatgcaatg catcatgcta ttctatacct aatgaggagg ttccaggaga ttcaaccagg 120  
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180  
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240  
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctctctg 300  
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

gttcctnnta actcctgcc aaaaacagctc tctcaacat gagagctgca cccctcctcc 60  
tggccagggc agcaagcctt agccttggtc tcttggttct gcttttttcc tggctagacc 120  
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180  
gtccattga cacctttccc actgaccca taaaggaaat ctcattggca caaggatttg 240  
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
gatatagaaa attcttgat gatcctata aacatgaaca ggtttatatt cgaagcacag 360  
acgttgaccg gactttgat agtgctatga caaacctggc agcccgctga cgcggccgag 420  
aatttagtag t 431

<210> 440  
 <211> 523  
 <212> DNA  
 <213> Homo sapiens

<400> 440  
 agagataaag cttagggtcaa agttcataga gttcccatga actatatgac tggccacaca 60  
 ggatccttttg tattttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
 tttaaatgtc tgaaatggaa cagattttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
 cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300  
 actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360  
 taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420  
 acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480  
 tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441  
 <211> 430  
 <212> DNA  
 <213> Homo sapiens

<400> 441  
 gtctctccta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60  
 tggccagggc agcaagcctt agccttggtt tcttgtttct gcttttttcc tggctagacc 120  
 gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180  
 gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240  
 gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
 gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360  
 acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420  
 aatttagtag 430

<210> 442  
 <211> 362  
 <212> DNA  
 <213> Homo sapiens

<400> 442  
 ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60  
 tttcctggaa tgacaattat attttaactt tgggtggggg aagagttata ggaccacagt 120  
 cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180  
 atgttttagaa atgggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240  
 aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300  
 tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360  
 tc 362

<210> 443  
 <211> 624  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(624)  
 <223> n = A,T,C or G

<400> 443  
 tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

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ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgagge ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgcta 480
agtagagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624
```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(425)

<223> n = A,T,C or G

<400> 444

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gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgttg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga 425
```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 445

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catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcatgtggc agattattgg atgtagtctt ctttaactag catataaact 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcctctec tcttgtattt tgaagcagtg 360
tggtgtgctg attgataaaa aaaaaaaaaa tcgacgcggc cgcgaattta gtag 414
```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(631)



<223> n = A,T,C or G

<400> 446

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tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtgggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg cattttgtgg 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

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ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtga gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

&lt;222&gt; (1) ... (706)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 449

```

ccaagttcat gctntgtgct ggacgctgga caggggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccatte gccattcagg ctgcgcaact 240
gttgggaagg gcgacgggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc caggggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgccactact tactaaattc gcggccgcgt 480
cgacgtggga tccncaactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

```

&lt;210&gt; 450

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

```

gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgatcc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcggcc 480
gcgaatttag tag 493

```

&lt;210&gt; 451

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 451

```

gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcgcc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcaca 360
cgcncacagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggcncctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(51)  
 <223> n = A,T,C or G

<400> 452  
 agacggtttc accnttataa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
 <211> 317  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(317)  
 <223> n = A,T,C or G

<400> 453  
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaacccat 120  
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
 taccatgtc tttatta 317

<210> 454  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 454  
 ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
 taagccacgc cagcctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
 agaagaccaa attccttctg atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180  
 ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 455  
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 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
 gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180  
 caaagaattt ctcatagcac agtcacaat acagggtctc tttctctct a 231

<210> 456  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 456  
 ttggcaggtg cccttataaa gaagacacca taccttatgc gttattaggt ggaataatca 60  
 ttccattcag tattatcggt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120  
 tgcactcaaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180

ccttttttatt tgggtgcagct gctagtcagtc ccctgactga cattgccaaag t 231

<210> 457  
<211> 231  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(231)  
<223> n = A,T,C or G

<400> 457  
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gcattccctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120  
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
agttgtctaa atcgatgcct catttctctt gaggtgtcgc tggcttttgt g 231

<210> 458  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 458  
agggtctggt cccccactt ccactccct ctactctctc taggactggg ctgggccaaag 60  
agaagagggg tgggttagga agccgttgag acctgaagcc ccacctcta ctttccctca 120  
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180  
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231

<210> 459  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 459  
ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60  
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120  
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180  
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 460  
gcagggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60  
cctatcacc ctttcttggg ggtgcttct tcacagtgat catgaagcct agcagcaaat 120  
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180  
gtggagcttg gtccagcctc cagtccacc ctaccaggct taaggataga a 231

<210> 461  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 461  
cgagggttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggaggggc 60

gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgctg tgtgtcctgg 120  
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180  
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60  
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120  
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

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catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180  
tggggagggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
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<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

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aggatggcac aatttttgct tgtgttcata atatactcag attagttcag ctccatcaga 180  
taaaactggag acatgcagga cattagggta gtgtgttagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

caggtaacct tttccattgg atactgtgct agcaagcatg ctctccgggg tttttttaat 60  
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaacat ttgcccagga 120  
cctgtgcaat caaatattgt ggagaattcc cttagctggag aagtcacaaa gactataggc 180  
aataatggag accagtccca caagatgaca accagtcggt gtgtgaggct g 231

<210> 467  
 <211> 311  
 <212> DNA  
 <213> Homo sapiens

<400> 467  
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 tgggtggcttt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120  
 tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180  
 gcatgggtct ctgcccgaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240  
 tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300  
 ctgcagcaga c 311

<210> 468  
 <211> 3112  
 <212> DNA  
 <213> Homo sapiens

<400> 468  
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 aagatctgca tgggtgggaag gacctgatga tacagagttt gataggagac aattaaaggc 120  
 tgggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180  
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 gtgaatgtgg atgattggat gatcatttct catctctgag cctcagggtc cccatccata 360  
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 atttgaagga tgaattgaga taatttatct cagggtccta gaacaatgcc cagattagta 480  
 catttgggtg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540  
 gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600  
 aaattgaact gttaacaaag gaatctctgg tcttgggtaa tggctgagca ccactgagca 660  
 tttccattcc agttggcttc ttgggtttgc tagctgcac actagtcac ttaaataaat 720  
 gaagttttaa catttctcca gtgatttttt tatctcacct ttgaagatac tatgttatgt 780  
 gattaaataa agaacttgag aagaacaggt ttcatataac ataaaatcaa tgtagacgca 840  
 aattttcttg atgggcaata ctatgttca caggaaatgc tttaaaatat gcagaagata 900  
 attaaatggc aatggacaaa gtgaaaaact tagacttttt tttttttttt ggaagtatct 960  
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 ttcgtgttgc tgcctaatat gtagctgact gtttttctta aggagtgttc tggcccaggg 2100  
 gatctgtgaa caggctggga agcatctcaa gatctttcca ggggttatac tactagcaca 2160  
 cagcatgatc attacggagt gaattatcta atcaacatca tcctcagtggt ctttgcccat 2220  
 actgaaatc atttcccact tttgtgcccc ttctcaagac ctcaaaatgt cattccatta 2280

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atatcacagg attaactttt ttttttaacc tggaagaatt caatgttaca tgcagctatg 2340
ggaatttaat tacatatattt gttttccagt gcaaagatga ctaagtcctt tatccctccc 2400
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tacagccaca gcctctccccc atccctccag ccttatctgt catcaccatc aaccctcccc 2520
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tctgcctgag aagctcttcc ttgtctctta aatctagaat gatgtaaagt tttgaataag 2640
ttgactatct tacttcatgc aaagaaggga cacatatgag attcatcatc acatgagaca 2700
gcaaatacta aaagtgtaat ttgattataa gagtttagat aaatatatga aatgcaagag 2760
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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

```

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aatggaatt

2229

&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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2426

&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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812

```

&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(515)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

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515

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&lt;210&gt; 473

&lt;211&gt; 5829

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 473

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aaaaaaaaa

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&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

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&lt;210&gt; 475

<211> 2414  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (33)  
<223> n=A,T,C or G

<400> 475  
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<210> 476  
<211> 3434  
<212> DNA  
<213> Homo sapiens

<400> 476

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<210> 478
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 478
Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
          5                      10                      15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
          20                      25                      30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
          35                      40                      45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
          50                      55                      60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
          65                      70                      75                      80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
          85                      90                      95

```



Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
5 10 15

Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
20 25 30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
35 40 45

Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
50 55 60

Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
65 70 75 80

Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
85 90 95

Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
100 105 110

Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
115 120 125

Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
130 135 140

```
<210> 481
<211> 167
<212> PRT
<213> Homo sapiens
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Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro  
5 10 15  
Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg  
20 25 30  
Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser  
35 40 45  
Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys  
50 55 60  
Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro



65		70		75		80									
Cys	Pro	Ala	Ala	Ser	Glu	Val	Gly	Gly	Cys	Ala	Pro	Ser	Ser	Trp	Arg
				85					90					95	
Ala	Leu	Ala	Glu	Val	Thr	Gly	Cys	Ser	Leu	Gly	Pro	Leu	Gly	Leu	Ala
			100					105					110		
Gln	His	Ala	Gln	Ala	Ser	Val	Leu	Leu	Leu	Cys	Tyr	Lys	Trp	Ser	His
		115					120					125			
Ile	Gly	Glu	Thr	Ser	Ser	His	Leu	Arg	Ser	Lys	Val	Tyr	Ala	Ala	Phe
	130					135					140				
Gly	Gly	Ser	Ser	Pro	Cys	Leu	Lys	Gly	Leu	Met	Ser	Leu	Trp	Ala	Ser
145					150					155					160
Trp	Leu	Ser	Arg	Gly	Arg	Pro									
				165											

<210> 482  
 <211> 143  
 <212> PRT  
 <213> Homo sapiens

<400> 482
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
5 10 15
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
20 25 30
Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
35 40 45
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
50 55 60
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
65 70 75 80
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
85 90 95
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
100 105 110
Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
115 120 125
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
130 135 140

<210> 483  
 <211> 143  
 <212> PRT

<213> Homo sapiens

<400> 483

```

Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30
Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95
Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110
Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125
Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

```

<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1      5              10              15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

```

<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

gggaagctta tcacctatgt gccgcctctg c

31

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486  
gcgaattctc acgctgagta ttggcc 27

<210> 487  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 487  
cccgattct tagctgccca tccgaacgcc ttcac 36

<210> 488  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 488  
gggaagcttc ttccccggct gcaccagctg tgc 33

<210> 489  
<211> 19  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 489  
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
1 5 10 15  
Ser Val Ala

<210> 490  
<211> 20  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 490  
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
1 5 10 15  
Leu Ser His Ser  
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<210> 491  
<211> 20  
<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
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Thr	Gly	Phe	Thr												
				20											

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
				20											

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
				20											

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
				20											

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro  
1 5 10 15  
Phe Pro Asn Gly  
20

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu  
1 5 10 15  
Pro Pro Pro Pro Ala  
20

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val  
1 5 10 15  
Ser Val Arg Val  
20

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val  
1 5 10 15  
Val Pro Gly Arg  
20

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Made in a lab

<400> 499

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 1           5           10           15
Ser Ala Phe Leu
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<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

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 1           5           10           15
Gly Ser Ile Val
                20
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<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

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Val Ser Ala Ala
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<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

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gaaaggccga ttnatnattn ccaaaacctn gaccacgggt gatttgaaaa tgaccagtcc      300
gacaaccgag gacacggcca cctatttttg tggcagaatg aatactggta atagtgggtg      360
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<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc\_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

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<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

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Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu
  1           5           10           15
Asn Ser Ala
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<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

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Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
  1           5           10           15
Asn Thr Ala Asn
                20
```

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

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atggagacag gcttgcgctg gcttctcctg gtcgctgcgc tcaaaggtgt ccagtgtcag      60
tcgctggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgc      120
accgtctctg gattctccct cagtagcaat gcaatgatct gggctccgcca ggctccaggg      180
aaggggctgg aatacatcgg atacattagt tatgggtgta gcgcatacta cgcgagctgg      240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt      300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg      360
ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa
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<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccagtgtcag 60  
 tcggtggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgt 120  
 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cggaactgg 240  
 gcaaaaggcc gggtcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgcgcactct gggcccaggc accctgggtc ccgtctcctt agggcaacct 420  
 aa 422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n = A,T,C or G

<400> 508  
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaaggtgtc cagtgtcagt 60  
 cgggtggagg gtccgggggt cgcctgggtc cgcctgggac acccctgaca ctcacctgca 120  
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattggta ctctgtgtga cacatactac gcgaggtggg 240  
 cgaaaggccg attcaccatc tccaaaacct cgaccacggg gcatntgaaa atcncagtc 300  
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15



<210> 511  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 511

Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Asp	Gln	Lys
1				5				10					15	

<210> 512  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 512

Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu
1				5				10					15	

<210> 513  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 513

Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Asx	Val	Tyr	Thr	Asn	Leu
1				5				10					15	

<210> 514  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 514

Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser
1				5				10					15	

<210> 515  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

&lt;400&gt; 515

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg  
1 5 10 15

&lt;210&gt; 516

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 516

Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln  
1 5 10 15

&lt;210&gt; 517

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 517

Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met  
1 5 10 15

&lt;210&gt; 518

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 518

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
1 5 10 15

&lt;210&gt; 519

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 519

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys  
1 5 10 15  
Gly

&lt;210&gt; 520

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 520

Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val	Pro	Arg	Ala	Glu	Pro	Gly	Thr
1				5					10					15	
Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly							
			20				25								

&lt;210&gt; 521

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20				25						30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
			35				40						45		

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg  
 145 150 155 160  
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

&lt;210&gt; 524

&lt;211&gt; 765

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 524

atggccacag caggaaatcc ctggggctgg ttcttggggt acctcatcct tgggtgtcgca 60  
 ggatcgctcg tctctggtag ctgcagccaa atcataaacg gcgaggactg cagcccgcac 120  
 tcgcagccct ggcaggcggc actgggtcatg gaaaacgaat tgttctgctc gggcgctcctg 180  
 gtgcacccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240  
 ctgggacctg acagtcttga ggccgaccaa gagccagggga gccagatggg ggaggccagc 300  
 ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360  
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcacacagcat tgcttcgcag 420  
 tgccctaccg cggggaactc ttgcctcggt tctggctggg gtctgctggc gaacggcaga 480  
 atgcctaccg tgctgcagtg cgtgaacgtg tcgggtggtg ctgaggaggt ctgcagtaag 540  
 ctctatgacc cgctgtacca cccagcatg ttctgcgccc gcggagggca agaccagaag 600  
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660  
 gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc cagggtgtcta caccaacctc 720  
 tgcaaatcca ctgagtggat agagaaaacc gtccaggcca gttaa 765

&lt;210&gt; 525

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 525

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

		35						40				45						
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln			
	50					55					60							
Trp	Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly			
65				70					75					80				
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met			
				85					90					95				
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu			
			100				105						110					
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu			
	115					120					125							
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala			
	130				135					140								
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg			
145				150					155					160				
Met	Pro	Thr	Val	Leu	Gln	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu	Glu			
			165					170						175				
Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys			
		180				185					190							
Ala	Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly			
	195					200					205							
Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly			
	210				215				220									
Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu			
225				230				235						240				
Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser					
			245					250										

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<210> 526
<211> 963
<212> DNA
<213> Homo sapiens
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<400>	526						
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aactgcatcg	tggctcttc	cgtaaaggacg	gaacgcagcc	tgcacgctcc	gatgtacctc	180	
tttctctgca	tgtttgcagc	cattgacctg	gccttatcca	catccaccat	gcctaagatc	240	
cttgcccttt	tctgggtttg	ttcccagagag	attagctttg	aggcctgtct	taccagatg	300	
ttctttatctc	atgccctctc	agccattgaa	tccaccatcc	tgctggccat	ggccttttag	360	
cgttatgtgg	ccatctgcc	cccactgcgc	catgctgcag	tgtccaacaa	tacagtaaca	420	
gccagatgtg	gcatcgtggc	tgtggctcgc	ggatccctct	ttttttccc	actgcctctg	480	
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caggatgtaa	tgaagttagc	ctatgcagac	actttgccc	atgtggtata	tggctcttact	600	
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gtgtcacaca	ttggtgtggt	actcgccttc	tatgtgccac	ttattggcct	ctcagttgta	780	
caccgcctttg	gaaacagcct	tcatcccat	gtgcgtggtg	tcatgggtga	catctacctg	840	
ctggtgcctc	ctgtcatcaa	tcccatcatc	tatggtgcc	aaaccaaaca	gatcagaaca	900	
cgggtgctgg	ctatgttcaa	gatcagctgt	gacaaggact	tgcaggctgt	gggaggcaag	960	
tga						963	

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<210> 527
<211> 320
<212> PRT
<213> Homo sapiens
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<400> 527



305 310 315 320

<210> 528  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 528  
actatgggtcc agaggctgtg 20

<210> 529  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 529  
atcacctatg tgccgcctct 20

<210> 530  
<211> 1852  
<212> DNA  
<213> Homo sapiens

<400> 530  
ggcacgagaa ttaaaaccct cagcaaaaca ggcatagaag ggacatacct taaagtaata 60  
aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 120  
tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180  
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240  
ttattgactt gcctgtgtta gaccggaaga gctggggtgt ttctcaggag ccaccgtgtg 300  
ctgcggcagc ttccgggataa cttgaggctg catcactggg gaagaaacac aytctgtgcc 360  
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420  
ggagtctctc cttcatagtt catccatag gctccagagg aaaattatat tattttgtta 480  
tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540  
ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 600  
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gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata 720  
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gatctcatcg tcatgctcag ggacacggat gtgaacaaga gggacaagca aaagaggact 1080  
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tgccaggaag atgaatgtgc gttaatgttg ctggaacatg gcactgatcc aaatattcca 1260  
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gcgaatttaa atgcgctgga tagatatgga agaactgctc tcatacttgc tgtatgttgt 1500  
ggatcagcaa gtatagtcag cctctactt gagcaaaatg ttgatgtatc ttctcaagt 1560  
ctggaaagac ggccagagag tatgctgttt ctagtcatca tcatgtaatt tgccagttac 1620  
tttctgacta caaagaaaaa cagatgttaa aaatctcttc tgaaaacagc aatccagaac 1680  
aagacttaaa gctgacatca gaggaagagt cacaagggt taaaggaagt gaaaacagcc 1740  
agccagagct agaagattta tggctattga agaagaatga agaacacgga agtactcatg 1800  
tgggattccc agaaaacctg actaacggtg ccgctgctgg caatggtgat ga 1852

<210> 531  
<211> 879

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

```

atgcatcttt catttcctgc atttcttctt ccctggatgg acagggggag cggcaagagc 60
aacgtgggca cttctggaga ccacaacgac tcctctgtga agacgcttgg gagcaagagg 120
tgcaagtggg gctgccactg cttccctcgc tgcaggggga gcggcaagag caacgtggtc 180
gcttggggag actacgatga cagcgccttc atggatccca ggtaccacgt ccatggagaa 240
gatctggaca agctccacag agctgcctgg tggggtaaag tccccagaaa ggatctcatc 300
gtcatgctca gggacacgga tgtgaacaag agggacaagc aaaagaggac tgctctacat 360
ctggcctctg ccaatgggaa ttcagaagta gtaaaactcg tgctggacag acgatgtcaa 420
cttaatgtcc ttgacaacaa aaagaggaca gctctgacaa aggccgtaca atgccaggaa 480
gatgaatgtg cgttaatgtt gctggaacat ggcactgac caaatattcc agatgagtat 540
ggaaataacca ctctacacta tgctgtctac aatgaagata aattaatggc caaagcactg 600
ctcttatacg gtgctgatat cgaatcaaaa aacaagcatg gcctcacacc actgctactt 660
gggtatacatg agcaaaaaa gcaagtgggt aaatttttaa tcaagaaaaa agcgaattta 720
aatgcgctgg atagatatgg aagaactgct ctcatacttg ctgtatgttg tggatcagca 780
agtatagtca gccctctact tgagcaaaat gttgatgtat cttctcaaga tctggaaaga 840
cggccagaga gtatgctgtt tctagtcac atcatgtaa 879

```

&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

```

Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
      5                      10                      15
Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
      20                      25                      30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
      35                      40                      45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
      50                      55                      60
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
      65                      70                      75                      80
Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
      85                      90                      95
Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100                     105                     110
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115                     120                     125
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      130                     135                     140
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
      145                     150                     155                     160
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165                     170                     175

```



Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu  
 180 185 190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu  
 195 200 205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu  
 210 215 220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu  
 225 230 235 240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys  
 245 250 255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp  
 260 265 270

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu  
 275 280 285

Val Ile Ile Met  
 290

<210> 533  
 <211> 801  
 <212> DNA  
 <213> Homo sapiens

<400> 533  
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 tatgccactg cagcattctt ggttgccaag aggccaaacca caggccatct tgagaaggag 180  
 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240  
 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300  
 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360  
 tctgcagggg tgcgtctgga ggaggtggac cagccacca ccttaccag tcaagggaagt 420  
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	245		250			255
Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg						
	260		265			270
Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met						
	275		280			285
Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys						
	290		295			300
Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn						
305		310		315		320
Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe						
	325		330			335
Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe						
	340		345			350
Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe						
	355		360			365
Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg						
	370		375			380

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg  
 385 390 395 400  
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr  
 405 410 415  
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser  
 420 425 430  
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly  
 435 440 445  
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro  
 450 455 460  
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln  
 465 470 475 480  
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly  
 485 490 495  
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala  
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 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile  
 515 520 525  
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn  
 530 535 540  
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp  
 545 550 555 560  
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu  
 565 570 575  
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His  
 580 585 590  
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp  
 595 600 605  
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly  
 610 615 620  
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln  
 625 630 635 640  
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu  
 645 650 655  
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly  
 660 665 670  
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu  
 675 680 685



Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr  
 690 695 700  
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu  
 705 710 715 720  
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser  
 725 730 735  
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly  
 740 745 750  
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr  
 755 760 765  
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu  
 770 775 780  
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys  
 785 790 795 800  
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn  
 805 810 815  
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu  
 820 825 830  
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu  
 835 840 845  
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile  
 850 855 860  
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg  
 865 870 875 880  
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr  
 885 890 895  
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp  
 900 905 910  
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp  
 915 920 925  
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr  
 930 935 940  
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val  
 945 950 955 960  
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala  
 965 970 975  
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met  
 980 985 990  
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995                      1000                      1005  
 Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro  
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 Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val  
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 Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu  
 1045                      1050                      1055  
 Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly  
 1060                      1065                      1070  
 Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu  
 1075                      1080                      1085  
 Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu  
 1090                      1095                      1100  
 Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile  
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 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp  
 1125                      1130                      1135  
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu  
 1140                      1145                      1150  
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr  
 1155                      1160                      1165  
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu  
 1170                      1175                      1180  
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile  
 1185                      1190                      1195                      1200  
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln  
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 20                      25                      30  
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser  
 35                      40                      45

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile  
 275 280 285  
 Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr  
 290 295 300  
 Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu  
 305 310 315 320  
 Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala  
 325 330 335  
 Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile  
 340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His  
 355 360 365  
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr  
 370 375 380  
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val  
 385 390 395 400  
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu  
 405 410 415  
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile  
 420 425 430  
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser  
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 Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val  
 450 455 460  
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly  
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 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln  
 485 490 495  
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile  
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 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg  
 515 520 525  
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr  
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 565 570 575  
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn  
 580 585 590  
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn  
 595 600 605  
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro  
 610 615 620  
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro  
 625 630 635 640  
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln  
 645 650 655  
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660					665					670					
Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln
	675						680					685			
Asp	Trp	Trp	Leu	Ser	Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val
	690						695					700			
Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp
	705					710					715				720
Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly
				725					730					735	
Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln
			740					745					750		
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu
		755					760					765			
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys
	770					775					780				
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe
	785					790					795				800
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala
			805						810					815	
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe
			820					825					830		
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg
		835					840					845			
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser
		850					855					860			
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys
	865					870					875				880
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe
			885						890					895	
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile
			900					905					910		
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala
		915					920					925			
Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu
		930					935					940			
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val
	945					950					955				960
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu
				965					970					975	

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp  
                   980                                  985                                  990  
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser  
                   995                                  1000                                  1005  
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser  
                   1010                                  1015                                  1020  
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser  
                   1025                                  1030                                  1035                                  1040  
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp  
                                   1045                                  1050                                  1055  
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys  
                                   1060                                  1065                                  1070  
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met  
                   1075                                  1080                                  1085  
 Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp  
                   1090                                  1095                                  1100  
 Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro  
                   1105                                  1110                                  1115                                  1120  
 Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val  
                                   1125                                  1130                                  1135  
 Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn  
                                   1140                                  1145                                  1150  
 Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr  
                                   1155                                  1160                                  1165  
 Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr  
                   1170                                  1175                                  1180  
 Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys  
                   1185                                  1190                                  1195                                  1200  
 Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr  
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 Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln  
                                   1220                                  1225                                  1230  
 Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg  
                   1235                                  1240                                  1245  
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&lt;212&gt; PRT

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<213> Artificial Sequence

<220>

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<211> 14

<212> PRT

<213> Homo sapiens

<400> 541

Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
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<211> 15

<212> PRT

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<211> 12

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<213> Homo sapiens

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Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val  
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<210> 544

<211> 18

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<213> Homo sapiens

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Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

199

5 10 15

Met Thr

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Ser Val

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Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
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Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu  
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Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys  
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Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
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200

5

10

15

Glu Cys

&lt;210&gt; 549

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 549

Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg  
5 10 15

Gln Ala

&lt;210&gt; 550

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 550

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe  
5 10

&lt;210&gt; 551

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 551

Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
1 5 10

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